PhD dissertation

Praca doktorska

Synthesis of chiral imidazolylidene ligands – potential asymmetry inductor of ruthenium, rhodium and palladium catalysts

Synteza chiralnych ligandów imidazolidenowych – potencjalnych induktorów asymetrii centrów katalitycznych rutenu, rodu i palladu

mgr inż. Agata Bajek

Promotors:

Prof. dr hab. inż. Stanisław Wołowiec (Rzeszow University)

Prof. Francis Verpoort (Ghent University)

RZESZÓW 2014

There is one thing even more vital to science than intelligent methods;

and that is, the sincere desire to find out the truth, whatever it may be.

Charles Sanders Peirce

Acknowledgements

During the course of the last five years, a number of people have provided valuable contributions, whom I would like to acknowledge.

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Table of Contents

Aim and scopes of PhD thesis

The work aimed at design and synthesis of chiral bidentate imidazolinium salts, able to coordinate to transition metal ions like ruthenium, rhodium and palladium. The chiral auxiliary ligands were expected to provide chiral surrounding of these metal ions by bidentate coordination through carbon and oxygen atoms. The attempts to synthesize complexes were performed in order to induce stereoselectivity of catalytic reactions in which the Ru(II), Rh(I) and Pd(II) complexes are involved. Current state of art within the subject of chiral ligands, catalytic complexes and catalytic processes is the matter of literature survey in introduction.

List of Abbreviations

Ad	1-adamantyl
Ar	aryl
BINAM	1,1'-binaphthalenyl-2,2'-diamine
BINAP	2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl
Bn	benzyl
Boc	*t*-butoxycarbonyl
bs	broad singlet
cod	cyclooctadiene
Cy	cycloxexyl
d	doublet
dba	*trans*, *trans*-dibenzylideneacetone
DCC	*N*,*N*'-dicyclohexylcarbodiimide
DCM	dichloromethane
DIPP	2,6-diisopropylphenyl
DMSO	dimethylsulfoxide
ee	enantiomeric excess
Et	ethyl
KHMDS	potassium bis(trimethylsilyl)amide
m	multiplet
Me	methyl
Mes	mesityl, 2,4,6-trimethylphenyl
Ms	mesyl or methanesulfonyl
NBS	*N*-bromosuccinimide
Ph	phenyl
Pr	propyl
Py	pyridine
q	quartet
R	alkil or aryl substituent
R*	chiral substituent
RCM	Ring Closing Metathesis
ROP	Ring-opening polymerization

s	singlet
SCE	saturated calomel electrode
t	triplet
*t*Bu	*t*-butyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TMS	trimethylsilyl
Ts	tosyl, *p*-toluenesulfonyl

Part 1

1. Literature survey

1.1 Introduction

N-heterocyclic carbenes (NHCs) are intriguing and long known singlet carbenes with the carbene incorporated in a nitrogen-containing heterocycle. The history of this interesting class of active species began in the early 1960`s after Wanzlick`s first studies on its reactivity and stability[1]. The first application of NHC as ligands for metal complexes was independently described by Wanzlick[2] and Öfele[3] in 1968. Afterwards, surprisingly, the field of NHCs as ligands in transition metal chemistry remained dormant until 1991 when Arduengo et al. reported first stable, crystalline 1,3-diadamantyl-2,3-dihydro-1*H*-imidazol-2-ylidene, IAd, by deprotonation of the corresponding imidazolium salt[4]. This deprotonation method was later complemented by Kuhn et al.[5] They use the reductive desulfurization of thiones for the preparation of stable imidazol-2-ylidenes.

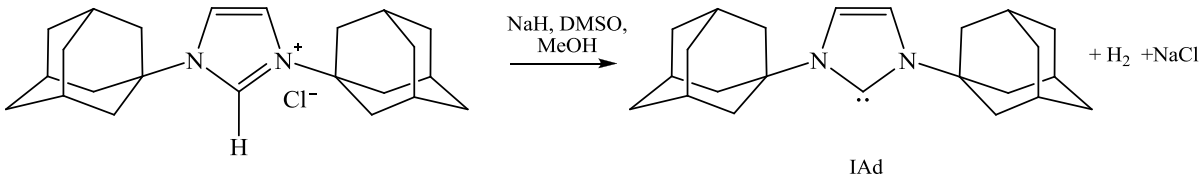


Fig. 1.1 Synthesis of first stable carbene.

The isolation of first stable *N*-heterocyclic carbene demonstrated that free carbenes were not necessarily unstable intermediate and triggered an intensive research for additional stable NHCs. That led to developing and isolation not only of the variety of NHC with different ring and *N*-substituents but also NHC derivatives with different heteroatoms in the carbene ring and different *N*-heterocyclic ring size.

Interesting features of *N*-heterocyclic carbenes such as their versatility, high electron donating ability and applicability in a broad range of transition metal mediated reactions

caused that this group of chemical compounds have become universal ancillary ligands in organometallic and inorganic coordination chemistry. General methods of their synthesis[6-10] as well as their coordination chemistry with metals[11-13] have already been reviewed. Its comprehensive and extensive applications including e.g.: olefin polymerization and metathesis by Ru-based catalysts[14,15], hydrosilylation by Rh and Pt carbene complexes[16], Ir-catalyzed hydrogenation and hydrogen transfer[17], Pd-catalyzed carbon-carbon coupling reactions[18] and increasing number of enantioselective reactions[19] are now well known. These types of reactions were traditionally carried out using phosphine-based systems but NHC complexes exhibit some more desirable properties not possessed by the former.

Since this work concerns synthesis and development of chiral, bidentate imidazolinium salts as NHC precursors for Ru, Rh and Pd complexes and their potential catalytic activity the literature part will be focused on synthesis of NHC complexes with those metal ions.

1.2 Synthesis of ligand precursors

Access to *N*-heterocyclic carbenes is mostly controlled by the availability of suitable NHC precursors. Most of them are obtained by deprotonation of corresponding azolium salts e.g.: imidazolium, imidazolinium, benzimidazolium, triazolium, thiazolium or by reductive desulfurization of imidazol-, benzimidazol-, imidazolin-2-thiones. A comprehensive overview of NHCs and their complexes synthesis has been given by Hahn et al.[20] On Fig. 1.2 are shown the most popular carbene moieties.

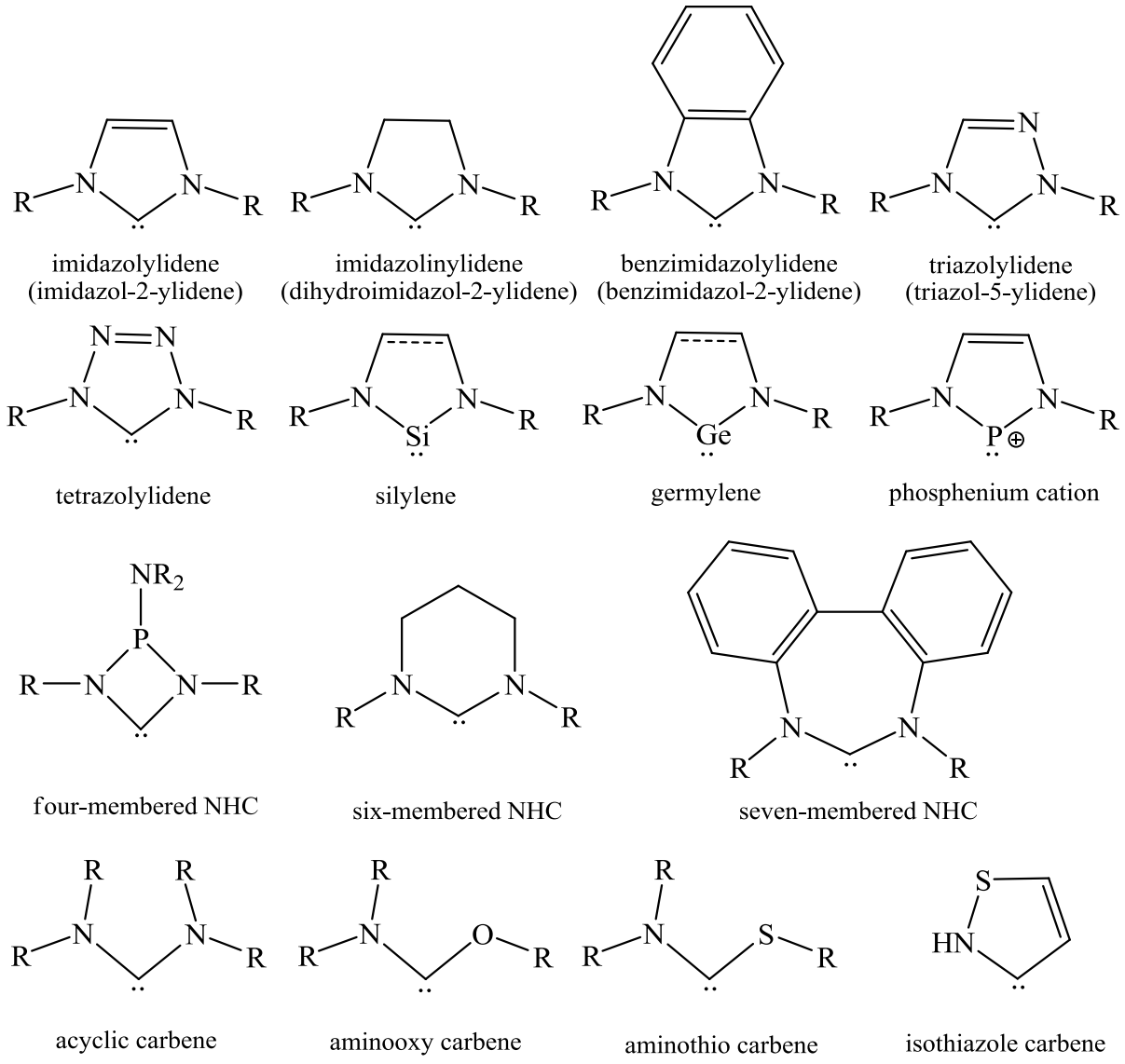
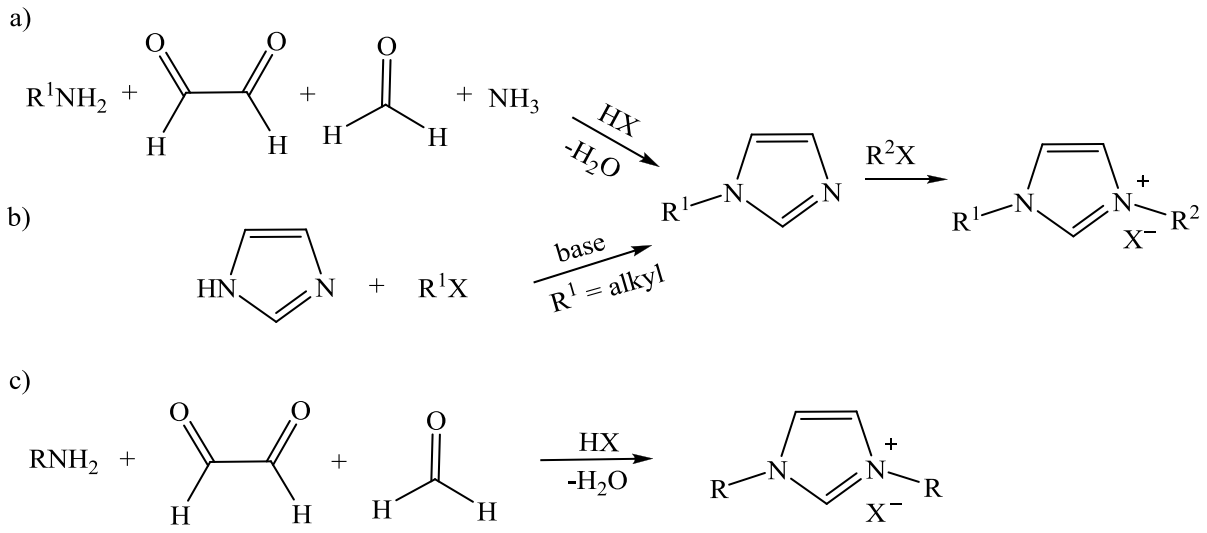


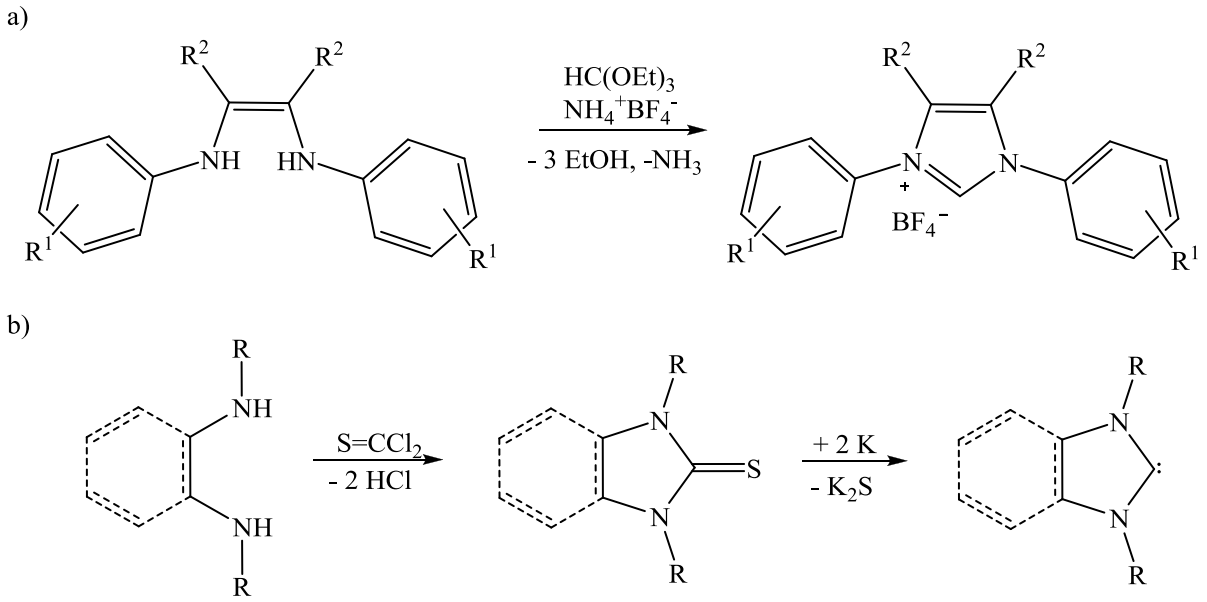
Fig. 1.2 Amino carbene frameworks.

The majority of *N*-heterocyclic carbenes are based on five-membered ring systems and the most important and most often employed *N*-heterocyclic carbenes are imidazol-2-ylidenes and the dihydroimidazol-2-ylidenes. Therefore special emphasis is placed on synthetic path leading to unsaturated and saturated NHC ligands featuring a five-membered diamino-heterocycle. Several methods have been described. Among them the alkylation of the nitrogen atoms of imidazole ring and building the imidazolium ring using symmetric or unsymmetrical synthetic procedure are two general methods (Scheme 1.1).



Scheme 1.1 General methods of synthesis of five-membered diaminoheterocycles.

However a lot of other synthetic routes have been developed and employed. Some of them are shown in Scheme 1.2 and shortly described below.



Scheme 1.2 Representative methods of synthesis of five-membered diaminoheterocycles.

A very useful and versatile method is the ring closure reaction of easily accessible 1,2-diamines into the aryl substituted imidazolium salts with orthoformate (Scheme 1.2 a).[21] The other interesting method is desulfuration of cyclic thiourea derivatives however it requires drastic conditions (Scheme 1.2 b).[22-24]

Almost immediately after the reports on the preparation of the first stable NHCs a lot of reports regard modified *N*-heterocyclic carbenes or their corresponding salts such as: *N*,*N*`-

donor functionalized[25-27], bridged bis- or tris-imidazolium[28-30], pincer ligands[31,32] or polydentate carbenes[33] appeared. Some examples of these salts are shown in Fig. 1.3.

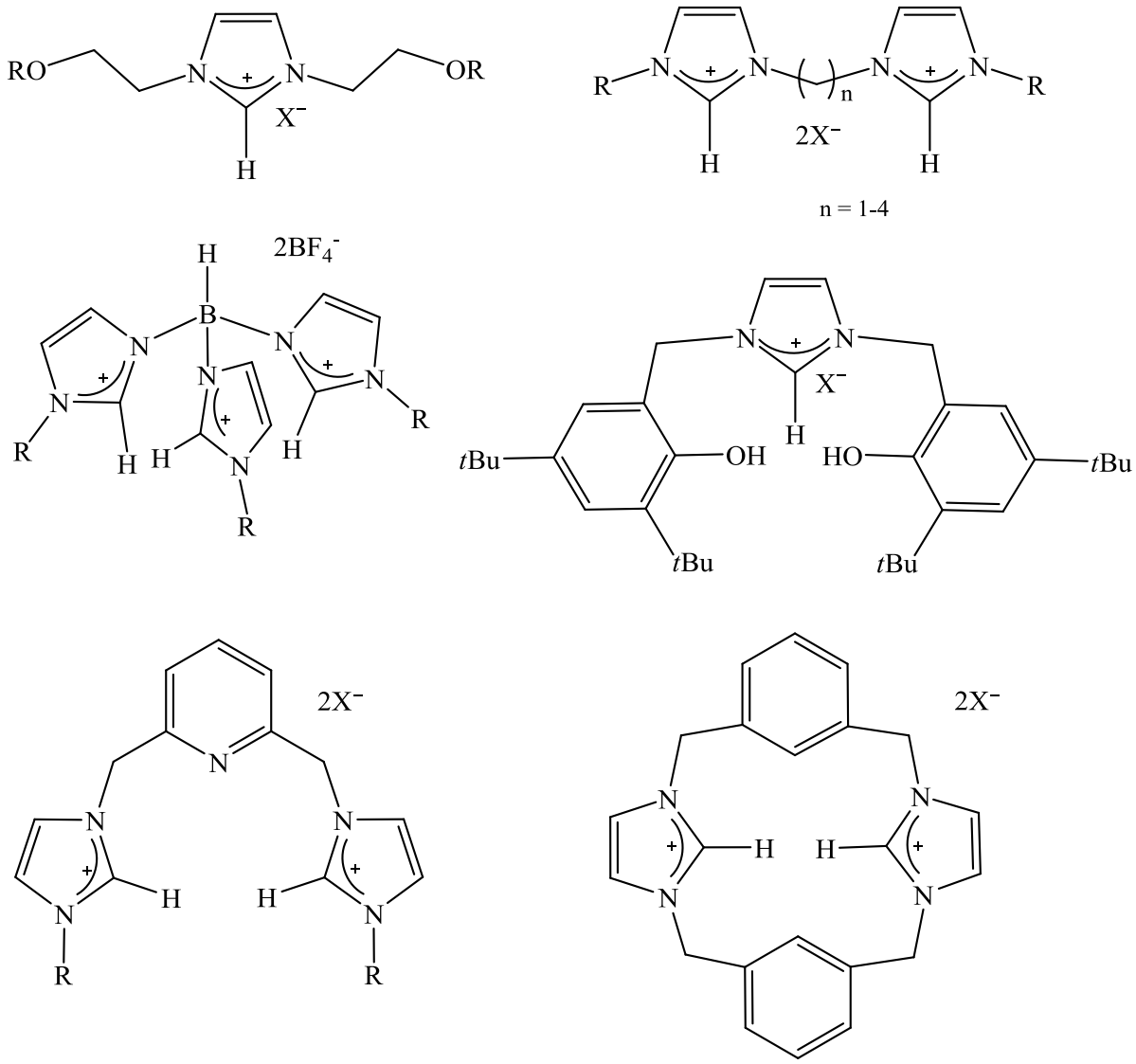


Fig. 1.3 Examples of modified *N*-heterocyclic carbenes precursors.

1.3 Synthesis of chiral *N*-heterocyclic carbenes precursors

Natural continuation in developing of the *N*-heterocyclic carbenes was synthesis of chiral precursors and their metal complexes used as catalysts in enantioselective transformations.

First attempts to use chiral NHC ligands in asymmetric catalysis started in the late 1990`s[34,35] but the rapid expansion of the field emerged not before publication by Burgess et al.[36] in 2001

that reported the first truly efficient chiral catalyst containing chiral NHC moiety. The number of reports regarding synthesis of chiral NHCs precursors and their metal complexes were grown instantly and have been continuously reviewed. In 2003 a first overview of chiral NHCs in catalysis was published by Burgess et al.[37] One year later a review by Gade et al.[38] appeared. This was followed up by reviews of synthesis and application of chiral NHC complexes in asymmetric catalysis by Mangeney et al.[39] in 2005, Gade et al.[40] and Douthwaite[41] in 2007 and most recently Shi et al.[42] in 2012.

The four types of stable diaminocarbenes used for the synthesis of chiral complexes are shown in Fig. 1.4.

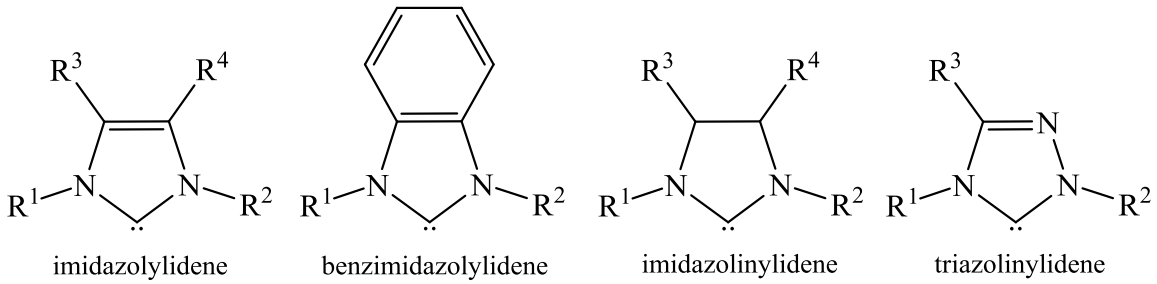


Fig. 1.4 Stable diaminocarbenes.

There are several available possibilities of introducing chirality into the *N*-heterocyclic carbene unit. It can be an asymmetric atom (central chirality), an axial chiral element (an atropisomeric substituent), planar chirality (planar chiral substituent) or their combinations. Gade et al.[38] proposed the division of NHCs derivatives into five main families. Among them NHC ligands with a stereogenic center on one or two *N*-substituents or within the *N*-heterocycle, NHC ligands containing an element of axial or planar chirality and finally carbenes incorporating oxazoline unit and NHC ligands combining the former types can be distinguish. This convention will be retained in followed part of this chapter.

1.3.1 *N*-heterocyclic carbene ligands with center of chirality on the *N*-substituents

The first strategy of designing the chiral NHCs concerned the introduction of *N*-substituents containing a stereogenic center. Their general structure is shown in Fig. 1.5.

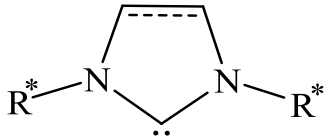


Fig. 1.5 General formula of the NHC ligands with chiral *N*-substituents.

The first chiral imidazolium salts of this type were synthesized using the methods described by Herrmann and Enders in 1996.[34,35] Symmetrical one were obtained using a one-pot condensation of chiral amines, paraformaldehyde and glyoxal under acidic conditions and the unsymmetrical are typically prepared by alkylating monosubstituted imidazoles with an appropriate alkyl halide. An imidazolium salt with an oxazoline unit was prepared by Herrmann, Burgess and Gade using the second method.[43-45] Subsequently reports on other examples of imidazolium NHC precursors emerged. Five step synthesis using L-proline as starting material[46] or an alkoxy-functionalized NHC obtained from a chiral epoxide[25] were prepared. Moreover Burgess et al.[47] and Douthwaite et al.[48,49] have reported the synthesis of mono- and bidentate NHCs using *trans*-cyclohexanediamine as a building block.

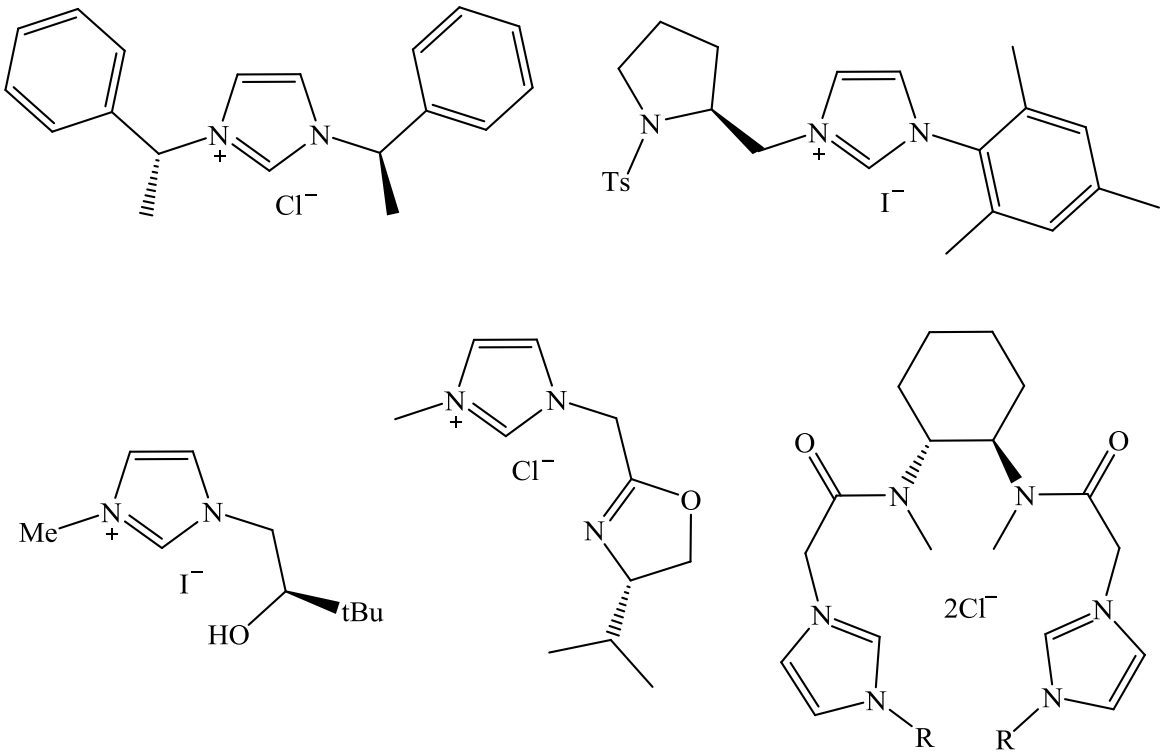


Fig. 1.6 Some examples of imidazolium salts with the stereogenic center on *N*-substituents.

Synthesis and development of 1,4-disubstituted triazolium salts prepared from alkyl or aryl hydrazines followed by addition of chiral amines and 1,3,4-trisubstituted triazolium

salts prepared by cyclization with acetic anhydride of the in situ prepared reaction of *N*-alkyl-*N*-formyl hydrazines with an imidoyl chloride were introduced by Enders et al.[50,51]. Simultaneously Leeper et al.[52] has developed triazolinylidene with a bicyclic moiety. This class of ligands was further investigated and the derivatives with stereogenic center introduced in the side chain remote from the carbon joined to the *N*-atoms of the ring and functionalized ones were reported.[53,54]

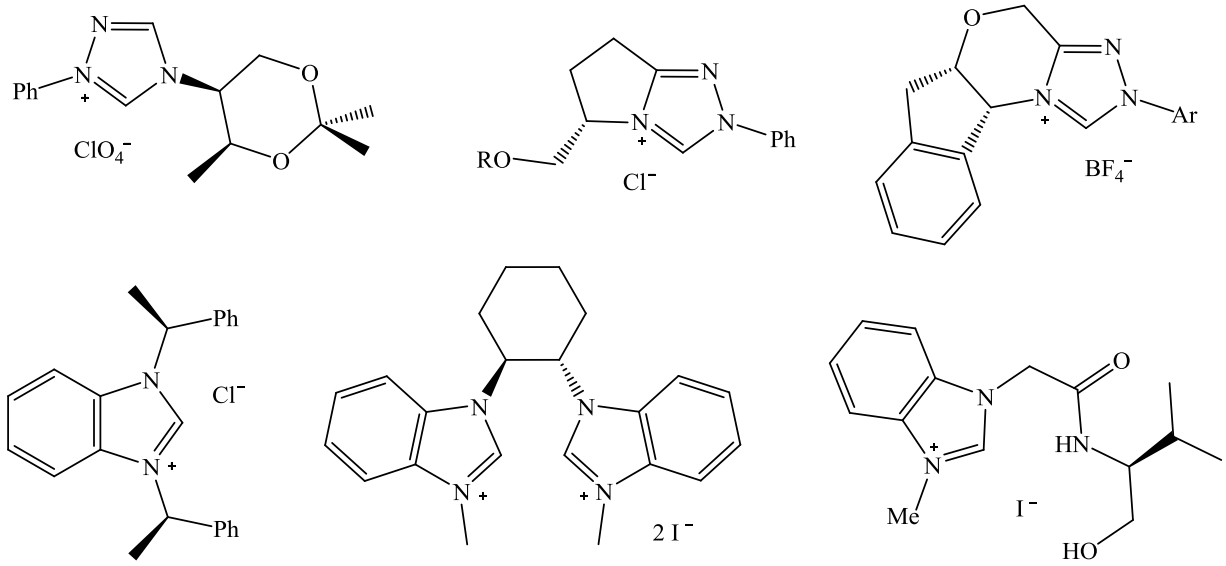


Fig. 1.7 Some examples of triazolium and benzimidazolium salts with the stereogenic center on *N*-substituents.

Diver et al.[55,56] reported synthesis of symmetrical and unsymmetrical chiral benzimidazolium salts starting from *o*-dibromobenzene. Later on in 2005 Shi et al.[57] reported the synthesis of racemic di-benzimidazolium salts obtained in four steps from (+/-) *trans*-cyclohexanediamine. Most recently the synthesis of chiral tridentate imidazolium salts using amino acids as starting material appeared.[58]

Design and development of imidazolinium salts with the center of chirality on *N*-substituents made also an important contribution to the field. (-)-Isopinocamphenylamine and (+)-bornylamine derivatives were synthesized by Hartwig et al. in 2001.[59] This group of NHC ligands will be further described in this dissertation (Chapter 1.4.2).

NHC ligands possessing chiral *N*-substituents that have been reported and studied to date generally gives moderate results in asymmetric catalysis. They are efficient stereodirecting ligands if the *N*-substituents are either sterically demanding or locked in fixed conformations. Functionalized, polydentate ligands or ligands combining the chirality

on *N*-substituents with other types of chirality may have higher potential in the stereoselective catalytic transformations.

1.3.2 *N*-heterocyclic carbene ligands with center of chirality within the *N*-heterocycle

The second family of chiral azolium precursors, that possesses a chiral center within the *N*-heterocyclic ring, is represented by imidazolinylidenes. This class of compounds contains sp^3-carbon atoms in the 4- and 5-position of the heterocycle therefore depending on the synthetic strategy one or two chiral center may be obtained (Fig. 1.8).

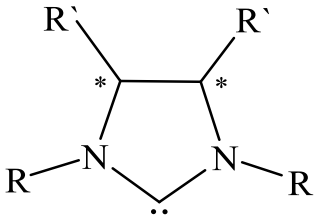


Fig. 1.8 General formula of the NHC ligands containing stereogenic centers within *N*-heterocycle.

This class of NHC ligands will be further and extensively described (Chapter 1.4.2).

1.3.3 *N*-heterocyclic carbene ligands with an element of axial chirality

A special case of chirality in which a molecule does not possess a stereogenic center but an axis of chirality is called axial chirality. The 1,1'-binaphthyl unit (shown in Fig. 1.9) is the most widely used structural moiety for the design of chiral ligands that convey asymmetric induction due to the configurationally stable atropoisomers formed as a result of the blocked rotation around the C-C axis linking the two naphthyl groups.[60] During exploration of NHC ligands the idea of incorporating an axial chirality to the azolium salts moieties has emerged. The first chiral NHC ligand containing a 1,1'-binaphthyl unit connected *via* methylene linkers with two imidazole rings was reported in 2000 by Rajanbabu et al.[61] Afterwards Shi et al.[62] have prepared in a four step synthesis starting from

enantiomerically pure BINAM the bidentate NHC ligand directly linked to the 1,1'-binaphthyl backbone (Fig. 1.9, right).

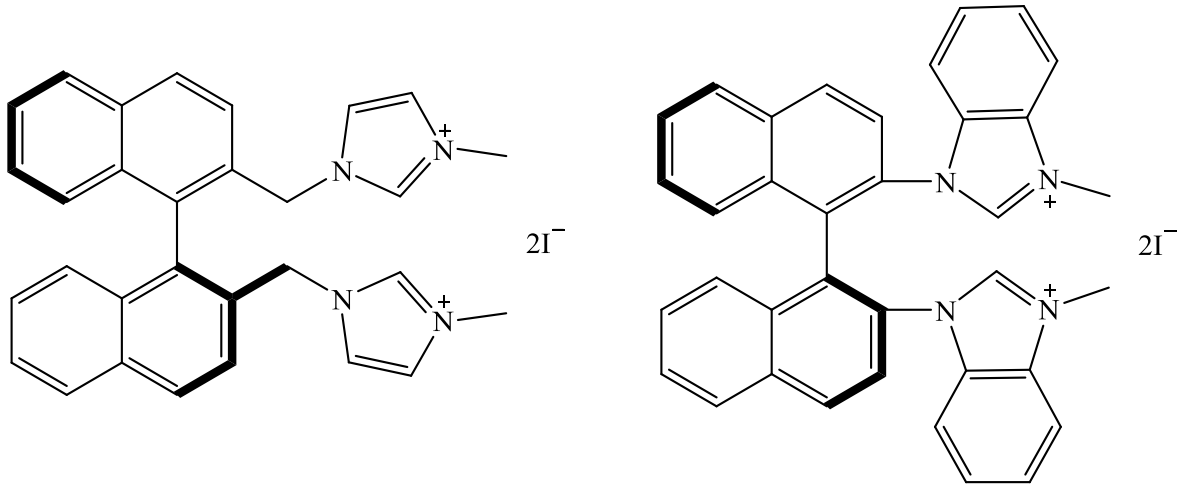


Fig. 1.9 Axial chiral bis-carbene ligands based on the 1,1'-binaphthyl scaffold.

Other interesting examples of this class of NHC ligands are reported by Hoveyda and Crabtree[63,64] anionic bidentate carbene ligand combining an NHC unit with a phenolato donor (Fig. 1.10, left) or reported by Herrmann et al.[65] carbene precursor with an axially chiral backbone made from benzannulated 1,1'-bipiperidine (Fig.1.10, right).

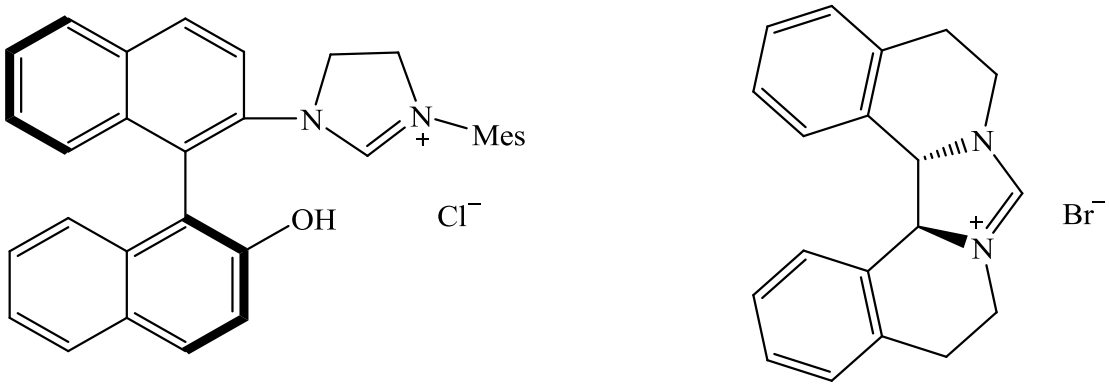


Fig. 1.10 NHC ligands containing phenolato donor and 1,1'-bipiperidine unit.

1.3.4 *N*-heterocyclic carbene ligands with an element of planar chirality

Synthesis and development of NHC ligands containing an element of planar chirality has also been investigated (Fig. 1.11). Synthetic strategy of the first planar chiral NHC ligands starting from a chiral sulfoxide was reported in 2002 by Bolm et al.[66] Shortly after

the chiral C_2-symmetric carbene containing both planar chirality in the ferrocenyl units and chiral centers at the carbon atoms linking the ferrocene with *N*-heterocycle starting from Ugi`s chiral 1-ferrocenylethylamine was published by Togni et al.[67] Three years later the same group reported synthesis of doubly ferrocenyl substituted imidazolium salt without the unnecessary methylene linker unit.[68]

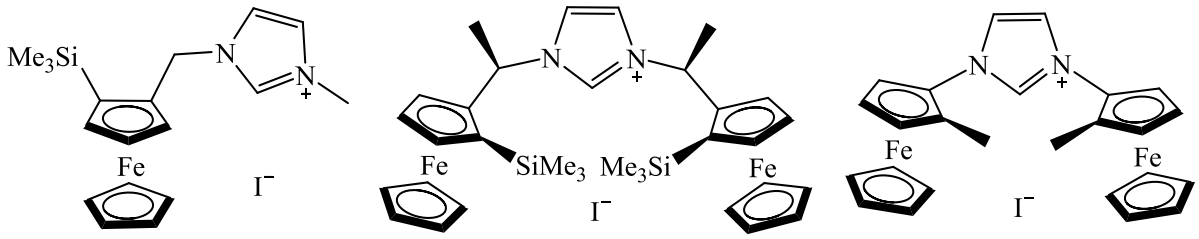


Fig. 1.11 Planar chiral and planar and central chiral, ferrocenyl (Fc) functionalized NHC ligands.

An imidazolium and imidazolinium based NHC ligands containing paracyclophanes as a chiral planar elements have also been developed.[69,70]

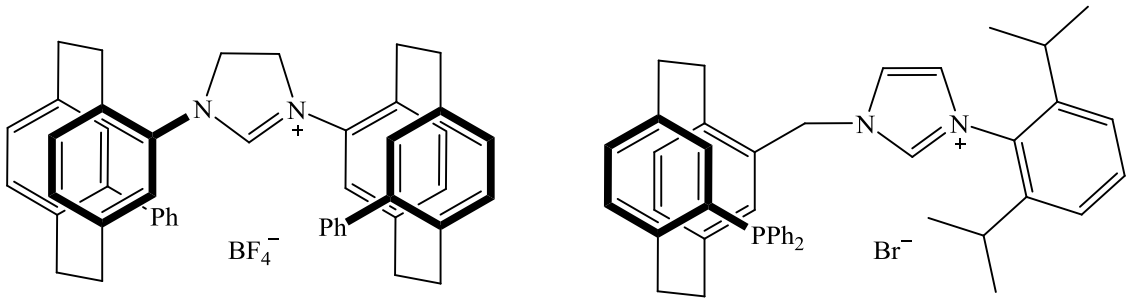


Figure 1.12 Planar chiral, [2.2]-paracyclophane functionalized NHC ligands.

1.3.5 Other possible chiral *N*-heterocyclic carbene units

Besides four previously mentioned families of NHC ligands the *N*-heterocyclic carbenes that combine in their structure two or more chiral elements of above mentioned types can be also marked out. They were mostly synthesized to obtain ligands that would possess potentially higher stereoselectivity towards selected reactions but also to expand the scope of this class of chemical compounds. Below in Fig. 1.13 a few examples of such more complex derivatives are shown.[71,72]

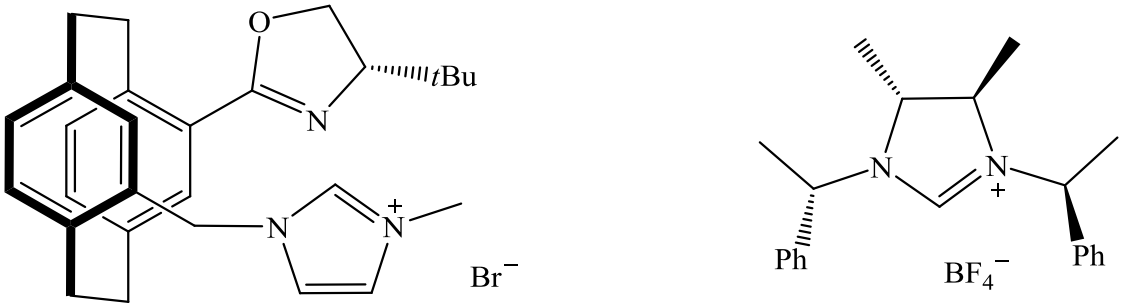
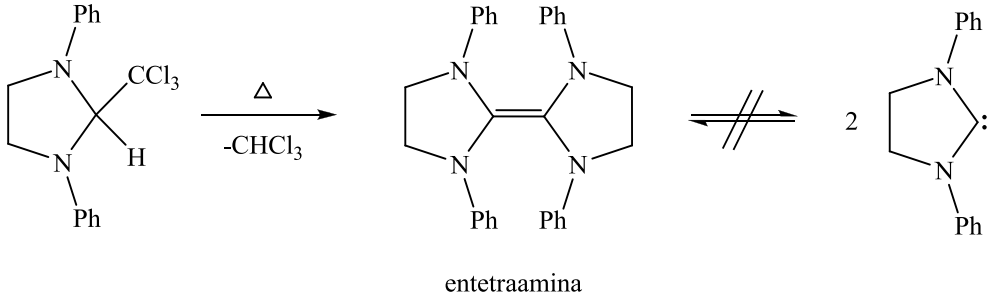


Fig. 1.13 Complex NHCs derivatives.

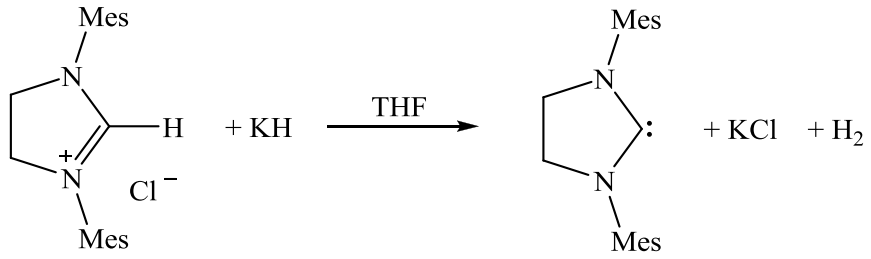
1.4 Development and design of imidazolinium salts

Recently, the saturated *N*-heterocyclic carbenes have received much attention, partially due to their increased Lewis basicity compared with their unsaturated counterparts.[11,73] Preparation of saturated imidazolin-2-ylidenes was first attempted by Wanzlick and Schikora[74] in early 1960. They have however reported synthesis of electron–rich vinyltetraamines instead of saturated carbenes *via* 1,1-elimination of chloroform from imidazoline derivatives.



Scheme 1.3 Wanzlick`s and Schikoras attempt to obtain saturated carbenes.

Once again Arduengo[75] was the first who has reported stable crystalline imidazolin-2-ylidene obtained by deprotonation of corresponding imidazolinium salt.

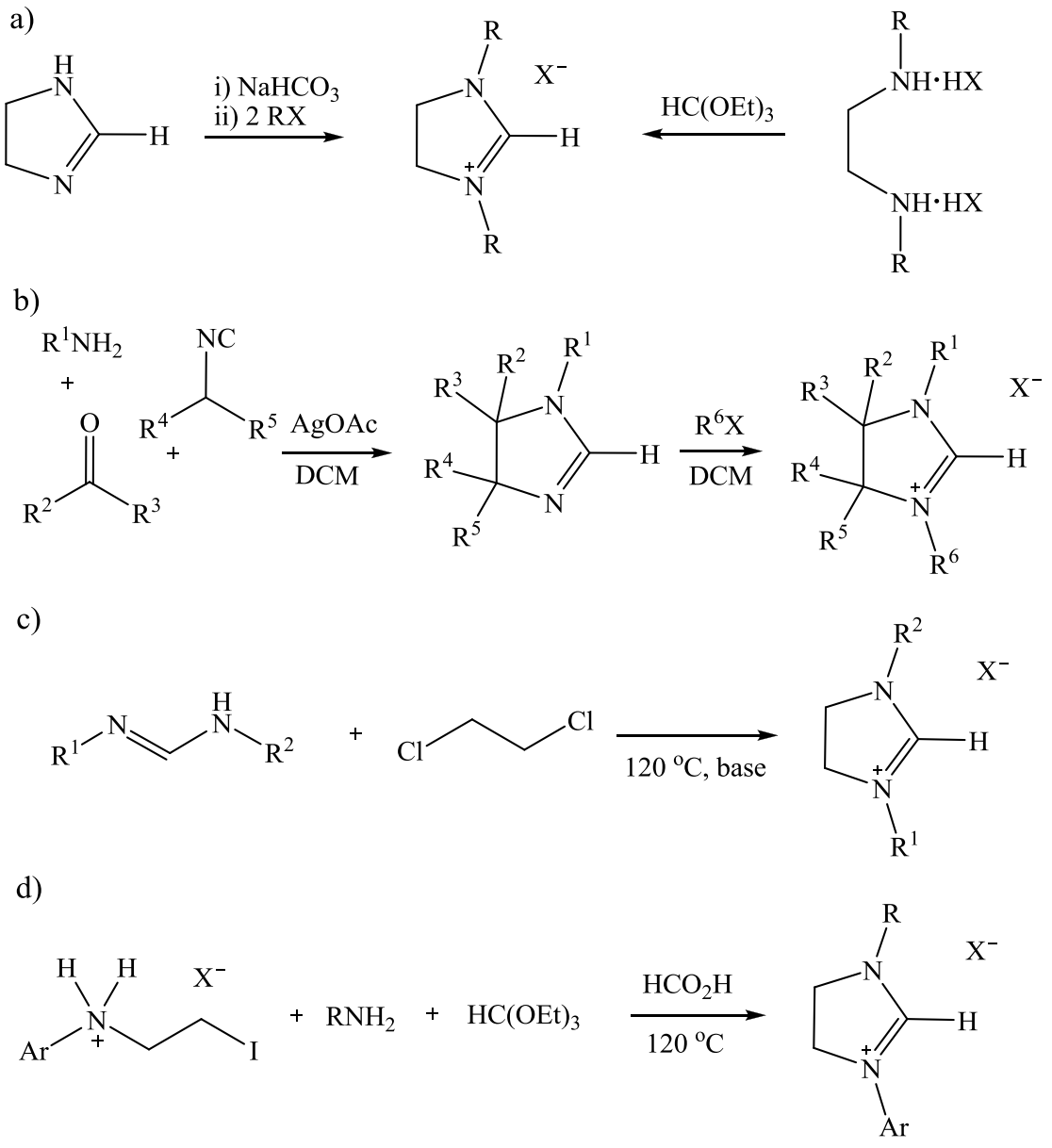


Scheme 1.4 Synthesis of first stable crystalline imidazolin-2-ylidene.

Carbenes obtained by reductive desulfurization of imidazolin-1-thiones that led to the *N,N'*-substituted stable carbene or to the entetraamine with sterically less demanding *N,N*'-substituents[23,76] and by 1,1-elimination reactions from imidazolidines[77,78] were also reporter thereafter.

1.4.1 Achiral imidazolinium salts

Saturated imidazolinium salts can be obtained using various complementary synthetic routes. These methods are summarized on Scheme 1.5.



Scheme 1.5 Synthetic routes for the preparation of imidazolinium salts.

Alkylation of dihydroimidazole or cyclization reactions between *N*,*N*'-dialkyl-α,β-ethyl-diamines with orthoesters that gives symmetric and unsymmetrical imidazolinium salts were reported at the earliest[21,79,80] (Scheme 1.5 a).

The synthesis based on so-called multicomponent reaction (Scheme 1.5 b) was reported and further developed by Orru and co-workers.[81-83] This reaction leads to unsymmetric imidazolinium salts with substituents at the C4 and C5 positions of heterocycle (Fig. 1.14).

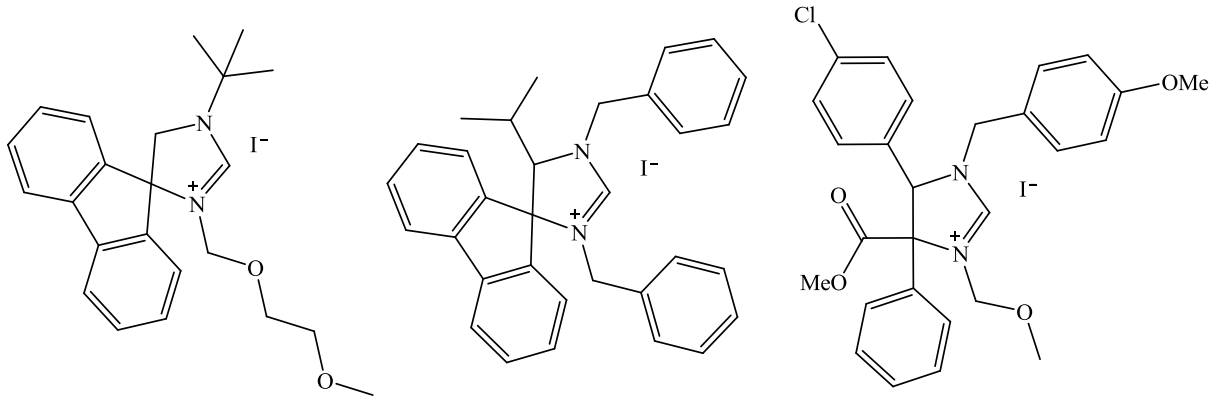


Fig. 1.14 Examples of imidazolinium salts obtained using multicomponent reaction.

Other approach, presented by Grubbs[84] who reported a facile synthesis of symmetric and unsymmetric imidazolinium chlorides, involves reaction of formamidine with 1,2-dichloroetane and base (Scheme 1.5 c and Fig. 1.15).

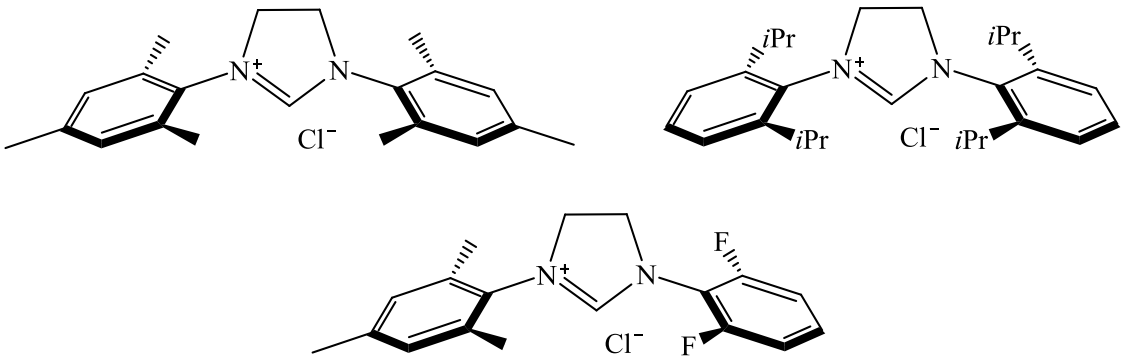
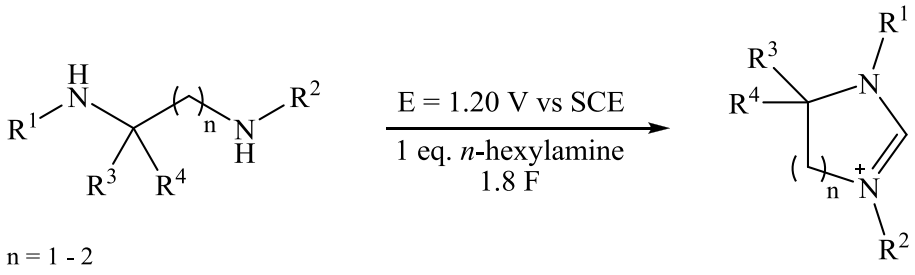


Fig. 1.15 Examples of imidazolinium chlorides obtained using above mentioned method.

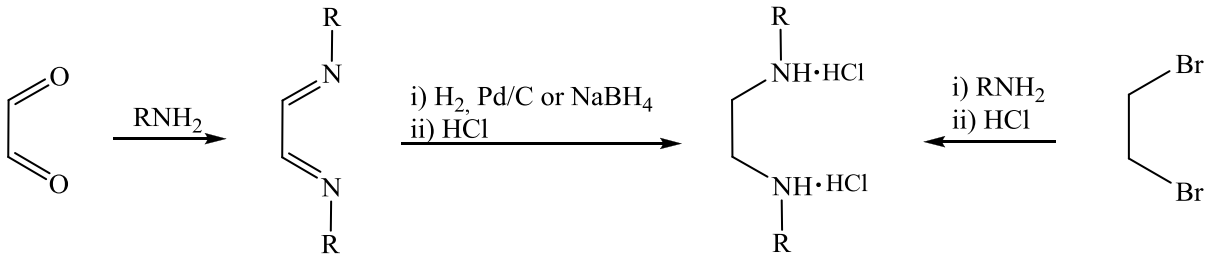
Interesting synthesis of various imidazolinium salts *via* reaction of stable *N*-(2-iodoethyl)-arylammonium salts with an amine and triethylformate was reported by Prasad et. al.[85] in 2009 (Scheme 1.5 d).

Moreover, in 2010 a one-pot electrosynthetic procedure giving imidazolinium cationic derivatives from secondary alkyl diamines in neutral media was reported.[86]



Scheme 1.6 Electrosynthetic procedure for obtaining imidazolium and tetrahydropyrimidinium cationic derivatives.

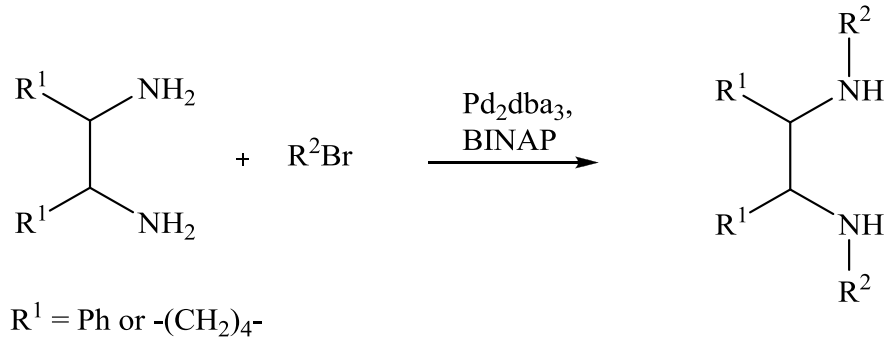
Although several synthetic routes were described the most of the reports regarding synthesis of imidazolinium salts are based on the general protocol shown in Scheme 1.5 a. Therefore number of synthetic routes leading to ethane-1,2-diamines have been developed and modified. The symmetric ones can be easily made *via* condensation of a variety of aromatic and aliphatic amines with glyoxal, followed by a reduction of the resulting Schiff bases[21,87] or alternatively *via* nucleophilic substitution of 1,2-dibromoethane with aromatic amines[88]. The second option is applicable to a broader range of substrates than the imine route.



Scheme 1.7 Synthesis of symmetrical 1,2-diamines.

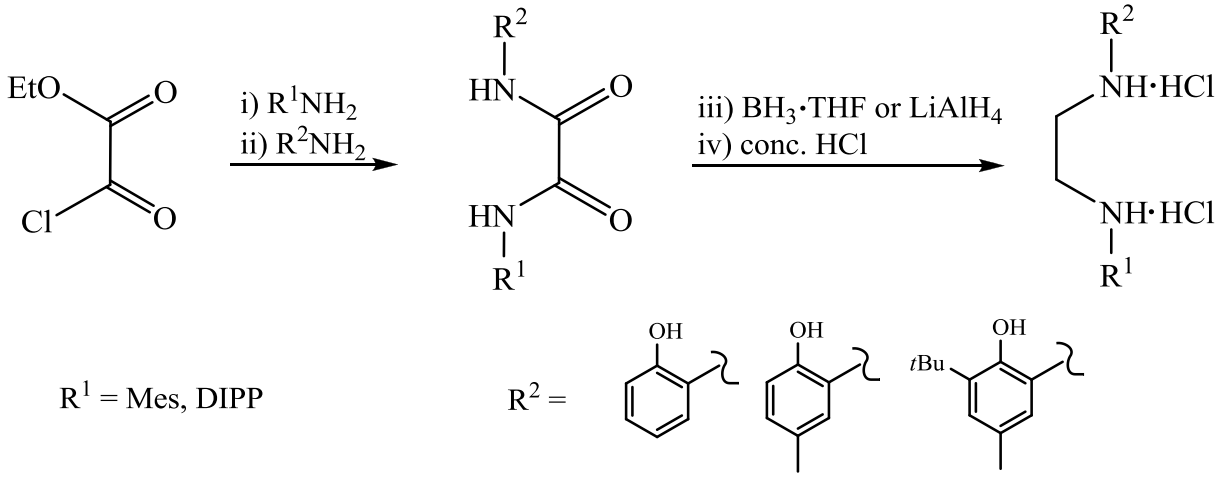
The synthesis of unsymmetric derivatives was also described using oxalyl chloride instead of glyoxal as starting material[89] or commercially available diamines[90].

One-step reaction of various aryl bromides with 1,2-disubstituted ethane-1,2-diamines *via* the Pd-catalyzed amination[91] was also introduced (Scheme 1.8).



Scheme 1.8 Synthesis of diamine precursors using Pd-catalyzed amination.

On the other hand reaction of ethyl-2-chloro-2-oxoacetate with two different amines to form an oxalamide, followed by reduction with BH_3·THF complex or $LiAlH_4$ that gives ethane-1,2-diamines (Scheme 1.9), which can be cyclized to form unsymmetrically, chelating *N*,*N*'-substituted imidazolinium salts were reported in 2004.[92,93]



Scheme 1.9 Synthesis of ethane-1,2-diamines.

During the last ten years many researching groups were developing and describing imidazolinium NHC precursors obtained using above mentioned approaches. And so report regarding synthesis of unsymmetric imidazolinium salts with aryl alkyl *N*-substituents and their Ru-complexes used as metathesis catalysts were reported by Blechert group[94] in 2006 (Fig. 1.16 a). Some new *N*,*N'*-bis(aryl)imidazolinium chlorides in which the *N*-aryl groups were substituted at the ortho and/or *para* positions with an alkyl or alkoxy group were reported shortly after[95] (Fig. 1.16 b). Palladium complexes with these saturated NHCs bearing cyclometalated aromatic substituents have shown good activity in the Heck coupling of aryl bromides with acrylates. At the same time Plenio group[96] reported synthesis of sulfonated,

water soluble imidazolinium salts (Fig. 1.16 c), which Pd-complexes were applied in aqueous Suzuki coupling reactions of aryl chlorides and synthesis of imidazolium and imidazolinium salts modified at the *para* position of aryl *N*-substituents with electron withdrawing substituents (Fig. 1.16 d) such as: -Et_3N^+, -SAr, –SO_2Ar, -Cl, -F, -Br.[97,98]

Symmetric and unsymmetric imidazolinium salts with *N*-aryl substituents were studied in Özdemir group.[99]

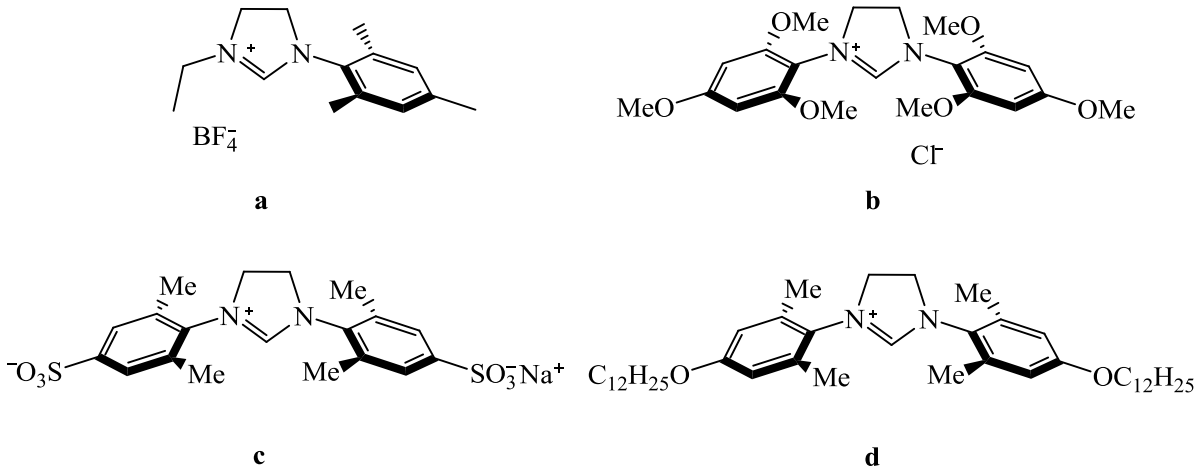


Fig. 1.16 Examples of functionalized imidazolinium salts.

Synthesis of easily accessible and stable imidazolin-2-ylidenes where the side chains were comprised of substituted naphthyl units have been reported by Dorta et al.[100,101] They have explored this class of NHC ligands, investigated their catalytic potential and studied the effect of substituents on the *syn-anti* conformer ratio. They have found that NHC ligands with bulky substituents on position 2 or 2,7 of the naphthyl chains display a very strong preference to assume only the *anti* conformation.[102]

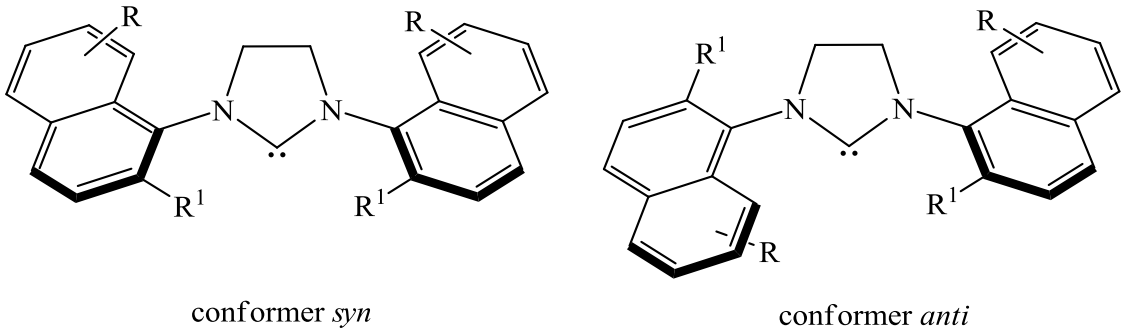
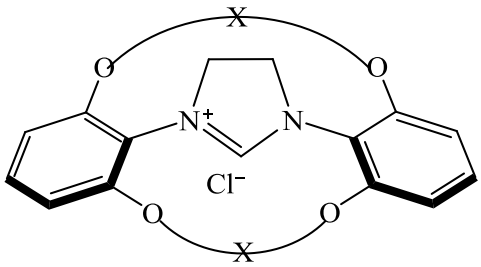


Fig. 1.17 *Syn* and *anti* conformers of naphthyl-based imidazolin-2-ylidenes.

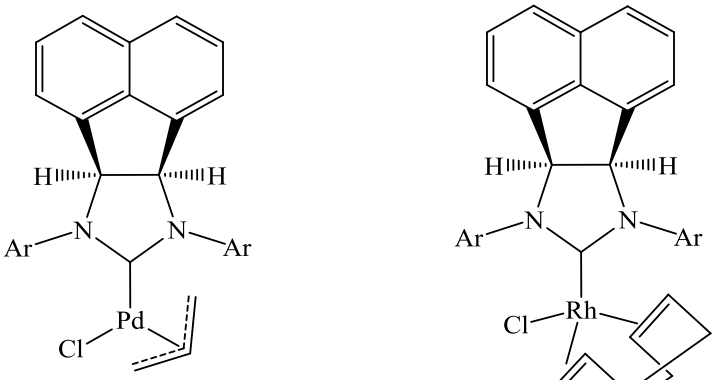
An interesting class of imidazolinium salts NHC precursors was reported by the group of Lüning.[103] They had described a synthesis of concave bimacrocyclic imidazolinium chlorides obtained in a six-step reaction where the macrocyclizations of concave reagents was performed using ring closing metathesis reaction (Fig.1.18). Subsequently, transition metal complexes of Ag, Cu, Pd, Rh and Ir using these salts as ligands, were reported. The reactivity of Pd-complex was investigated in Mizoroki-Heck and Suzuki-Miyaura cross-coupling reactions giving comparable activities to the related non-macrocyclic palladium allyl complexes.[104,105]



X = $(CH_2)_8$, $(CH_2)_{10}$

Fig. 1.18 General structure of concave imidazolinium salts.

Annulated diaminocarbenes have also been studied. Reports by Çetinkaya et al. and further by Dastgir and Green present the Ag-, Pd-,Rh- Ir-complexes containing this class of NHC ligands (Fig. 1.19).[106] Rh-complexes were tested for the hydroformylation of 1-octene and Pd-complexes have been tested for Suzuki coupling reaction and aryl amination reaction of activated and deactivated aryl halide.



Ar = 2,4,6-trimethylphenyl, 2,6-diisopropylphenyl

Fig. 1.19 Rh-, Pd-complexes containing annulated diaminocarbenes.

The exploration of the field of imidazolinium-based NHC precursors was continued by Plenio group[107], who obtained high molecular weight imidazolinium salts(800 and 1100

g/mol) with bulky $–CH_2NCy_2$ substituents (Fig. 1.20). This mass-tagged ligands were used to generate Ru-complexes which catalytic activity towards olefin metathesis reactions was tested giving slightly superior results comparing to their smaller analogues and moreover could be efficiently recovered from a reaction mixture by a single nanofiltration. Whereas catalytic activity of Pd-complexes with general formula (NHC)Pd(allyl)Cl and (NHC)Pd(cinnamyl)Cl were tested in the Suzuki-Miyaura coupling and Buchwald-Hartwig amination. Solvent-resistant nanofiltration enabled to obtain Pd recovery up to 99.9% in a double-filtration experiment.[108]

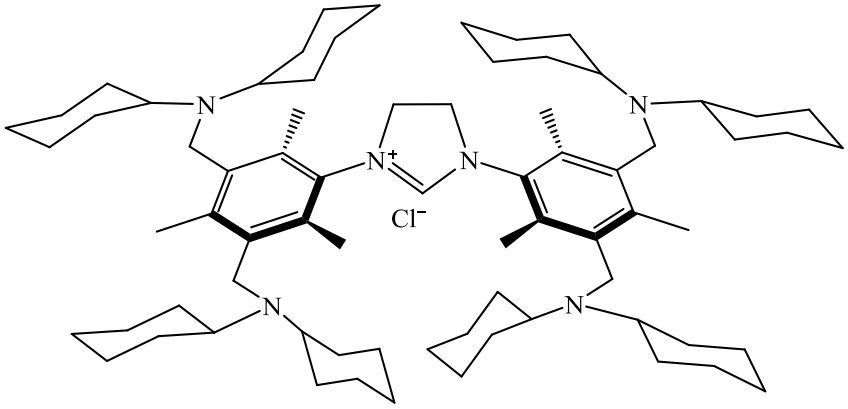


Fig. 1.20 Enlarged imidazolinium salts containing $–CH_2NCy_2$ substituents.

Other sterically demanding imidazolinium salts with enlarged *N*-substituents or enlarged substituents within the *N*-heterocycle were reported more recently.[109,110] Ru-complexes containing this enlarged ligands were tested for Ring Closing Metathesis, RCM, and Cross Metathesis, CM, reactions.

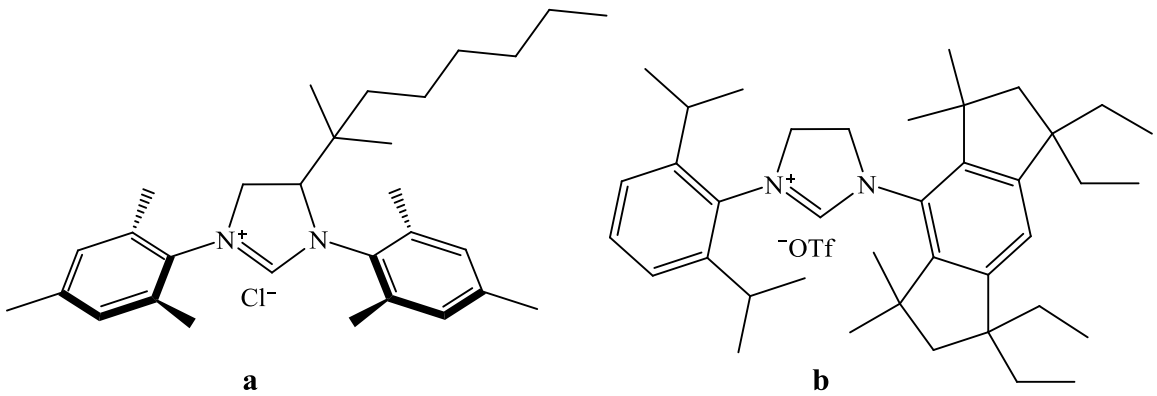


Fig. 1.21 NHC salts: a) with enlarged substituents within heterocycle and b) with enlarged *N*-substituents.

Attempts to obtain functionalized pincer systems of the type PCP and NCN wherein the central carbon donor is a saturated NHC ligand were undertaken. Fryzuk et al.[111] reported the synthesis of imidazolinium diphosphine ([PCP]H)PF_6 followed by reaction with group 10 M(0) reagents giving Ni, Pd, Pt hydride complexes [(PCP)MH]PF_6. Moreover most recently Thomas et al.[112] reported that NHC-ligated metal-hydride species are obtained if the halide-free imidazolinium salt is used but the imidazolinium C-H bond remains intact when imidazolinium chlorides are used. Yiğit et al.[113] described synthesis of picolyl substituted imidazolinium hexafluorophosphate salts and their use in Pd-catalyzed Heck reaction of aryl bromides with styrene, whereas Le Roux[114] reported synthesis of tridentate NCN chelating NHC zinc complexes.

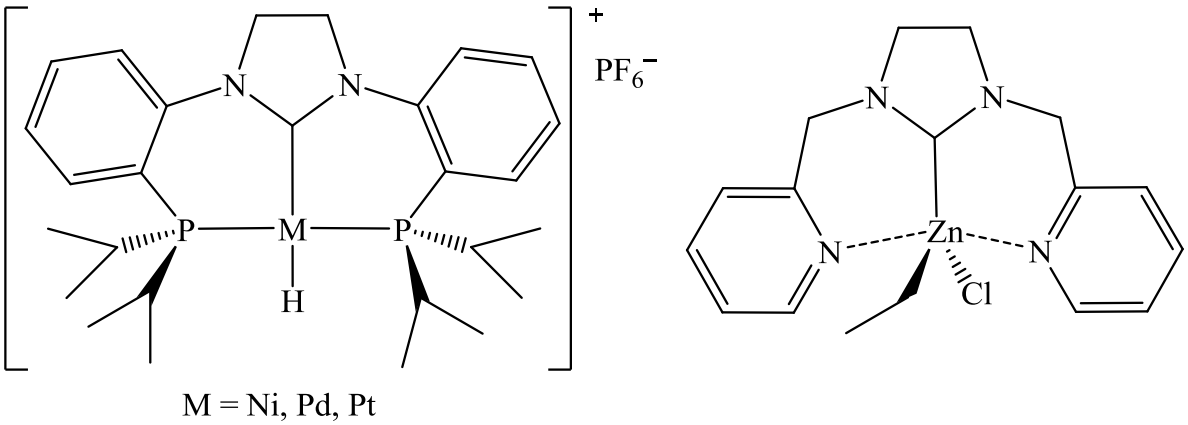


Fig. 1.21 Examples of PCP and NCN pincer systems containing saturated NHC.

Titanium complexes bearing a tridentate bis-phenolate-*N*-heterocyclic carbene dianionic ligands tested in controlled ring-opening polymerization reaction, of *rac*-Lactide[115] were reported and functionalized azolin-2-ylidene Pd-complexes were also described.[116]

Biscarbene Ru- and Rh-complexes[117] and mono-, bis-, and tris-piperidine fused imidazolinium salts[118] have also been developed and described.

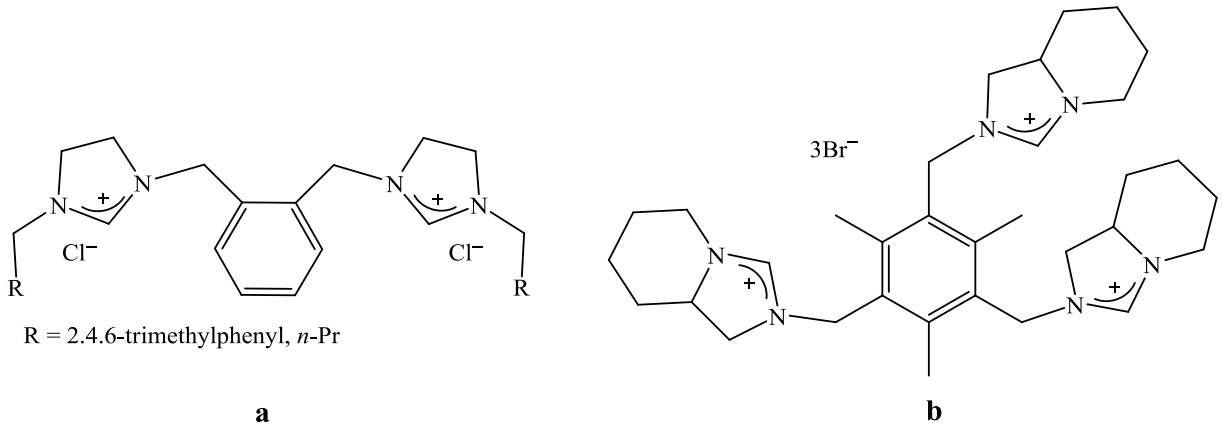
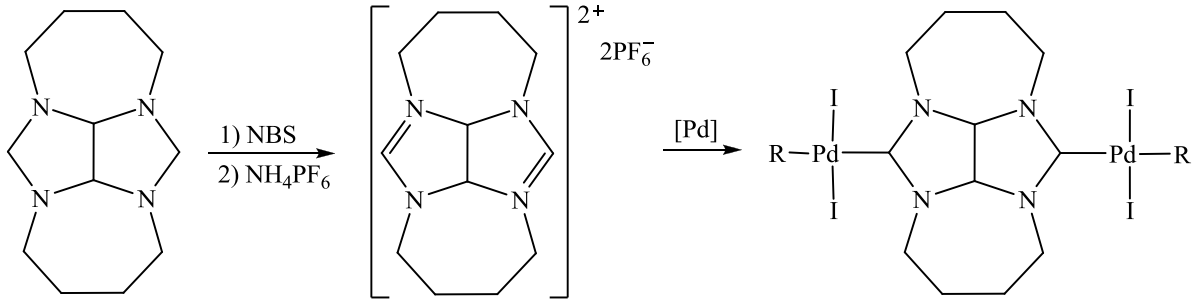


Fig. 1.22 a) Biscarbene xylyl linked imidazolinium salt, b) trisipiperidine fused imidazolinium salt.

Moreover bisimidazolindiylidenes ligands and tetracyclic bisimidazolindiylidenes ligands and their diiridium and dipalladium complexes which catalytic activity toward acylation reaction of aryl halides with hydrocinnamaldehyde were tested[119] or imidazolinium salts bearing a long spacer coordinated to Ru-complexes used as catalyst in olefin metathesis reactions were reported most recently[120].



Scheme 1.10 Synthesis of tetracyclic bis(imidazolinium) salt and its dipalladium complex.

This short overview shows different classes of imidazolinium salts that have been developed, synthesized and reported so far. Most of them were coordinated to the metal center giving metal-complexes that could serve as useful catalyst for several reactions among which C-C coupling reactions are the most abundant. The structure modification could alter the coordination behavior of these ligands and thereby provide the opportunity for catalysts fine tuning.

1.4.2 Chiral imidazolinium salts

The field of imidazolinium salts as NHC ligands precursors was expanded likewise to other types of auxiliary ligands for their chiral analogs since the chiral ligand could serve as useful chirality center within metal complex and therefore induce stereoselectivity. Saturated NHC ligands could possess stereogenic centers in C4 and C5 position on the backbone, on the nitrogen substituents or could be a combination of both of them.

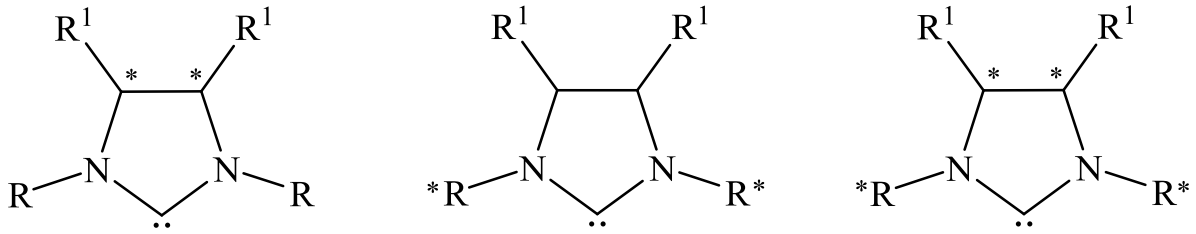


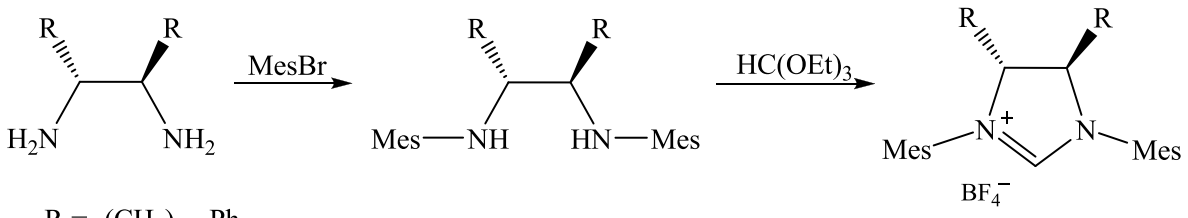
Fig. 1.23 Possible stereogenic centers within chiral saturated NHCs.

In this chapter the chiral imidazolinium salts will be divided into three groups depending on the denticity of a single ligand.

1.4.2.1 Monodentate imidazolinium salts

Synthesis of saturated NHC ligands possessing stereogenic centers in the imidazole ring (endocyclic chirality) or in the wingtip groups (exocyclic chirality) is based on a few synthetic protocols partially described in preceding chapters.

The commercially available (1*R*,2*R*)-1,2-diaminocyclohexane and (1*R*,2*R*)-diphenylethylenediamine[121] or chiral amines [34,122] were applied to obtain imidazolinium salts at first.



R = -$(CH_2)_4$-, Ph

Scheme 1.11 Synthesis of chiral saturated NHC precursors starting from chiral diamines.[121]

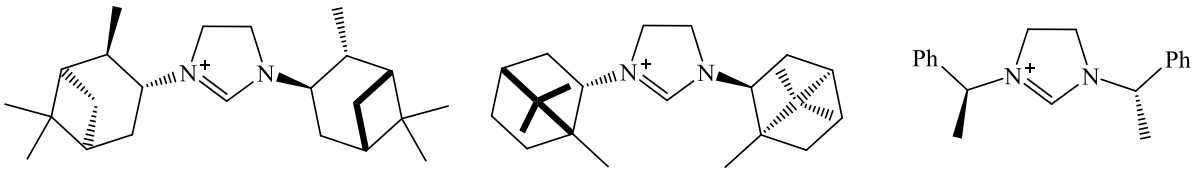
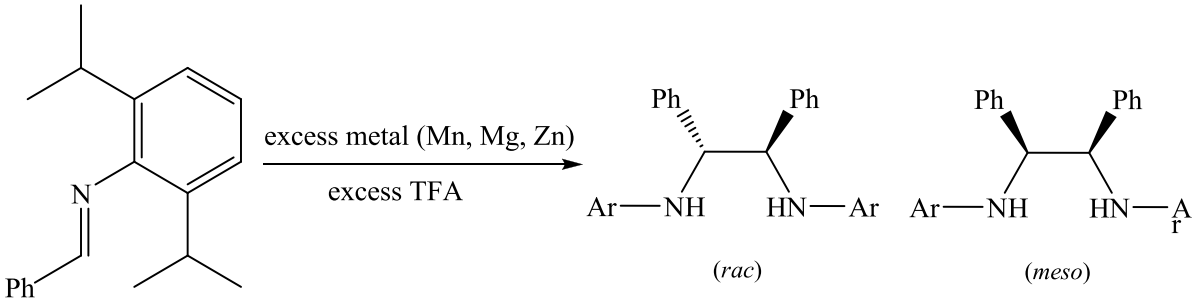


Fig. 1.24 Saturated NHC ligands from (-)-isopinocamphenylamine, (+)-bornylamine and phenethylamine.[34,122]

Synthesis of hindered *N*-aryl diamines using method presented in Scheme 1.11 appeared to be inefficient therefore an alternative method using reductive dimerization of a Schiff base by a base metal in the presence of trifluoroacetic acid giving a mixture of diastereoisomers was introduced (Scheme 1.12).[123]

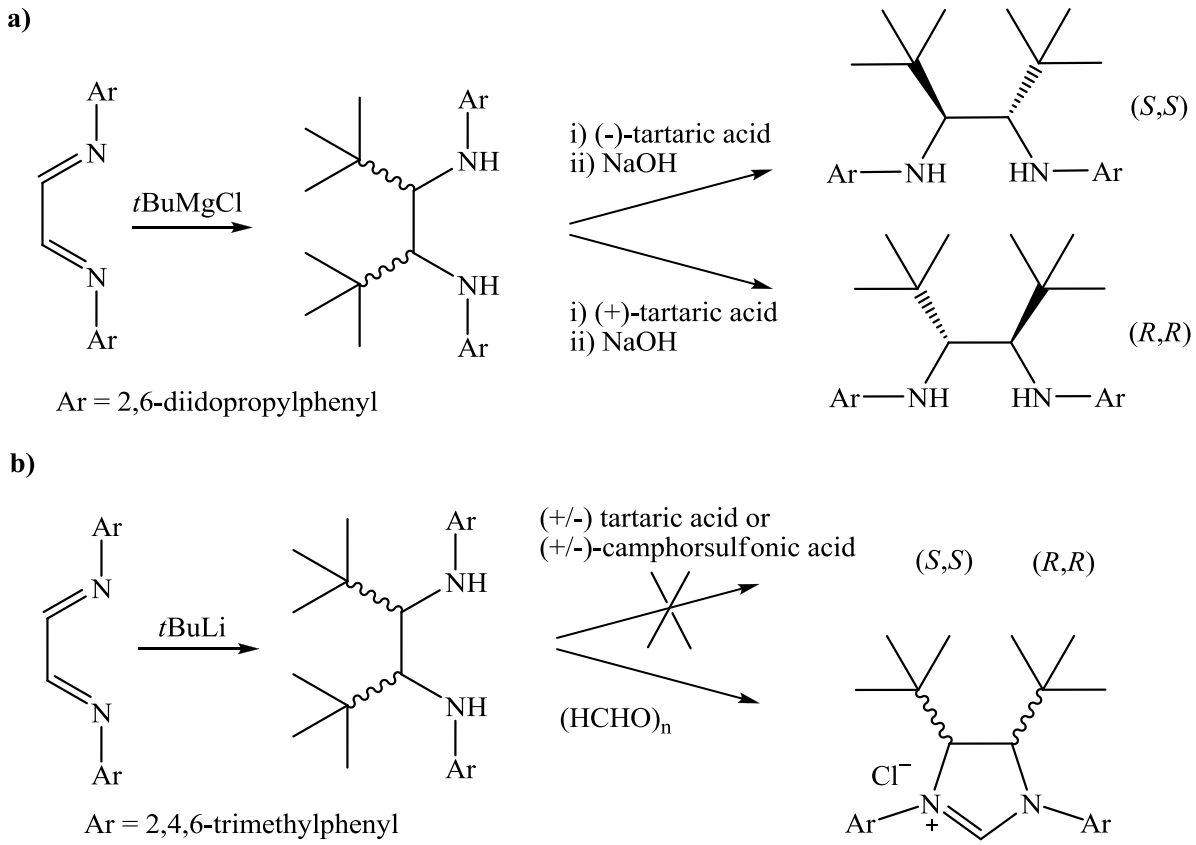


Scheme 1.12 Synthesis of bulky chiral 1,2-diamines using reductive dimerization.

More recently a range of symmetric imidazolinium salts with different *N*-substituents starting from (1*R*,2*R*)-cyclohexane-1,2-diammonium mono-(+)-tartrate were prepared. Their reactivity and asymmetric induction as catalyst for the asymmetric synthesis of *β*-lactams was tested and evaluated.[124]

Preparation of chiral imidazolinium salts bearing *tert*-butyl groups on the backbone was also investigated. First attempt was performed by Pytkowicz et al[125] by oxidation of the (*R*,*R*)-4,5-di-*tert*-butylimidazoline in the presence of palladium hydroxide and ammonium formate. Using of (1*R*,2*R*)-di-*tert*-butyl ethylenediamine to obtain unsymmetric chiral imidazolinium salt was reported by Fournier et al.[126] A different approach was provided by Zinner et al.[127] who synthesized enantiomerically pure imidazolinium salts starting from corresponding diimine. Chirality was introduced using a Grignard reagent followed by chiral resolution of the racemic mixture as the diamine tartrate and their final liberation with NaOH (Scheme 1.13 a).

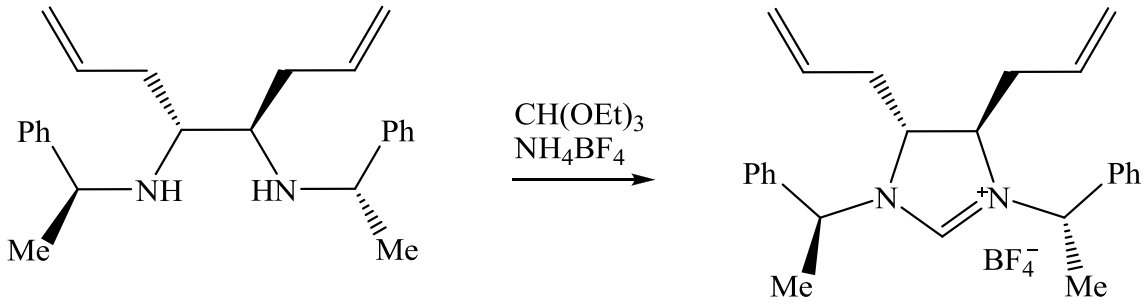
Synthesis of racemic imidazolinium salts with *tert*-butyl substituents in the heterocyclic backbone obtained by the addition of *tert*-butyl lithium on symmetrical 1,2-bisimines was reported most recently however the resolution of racemic solution was unsuccessful (Scheme 1.13 b).[128]



Scheme 1.13 Synthesis of chiral 1,2-diamines and imidazolinium salts with *t*Bu substituents in the heterocycle.

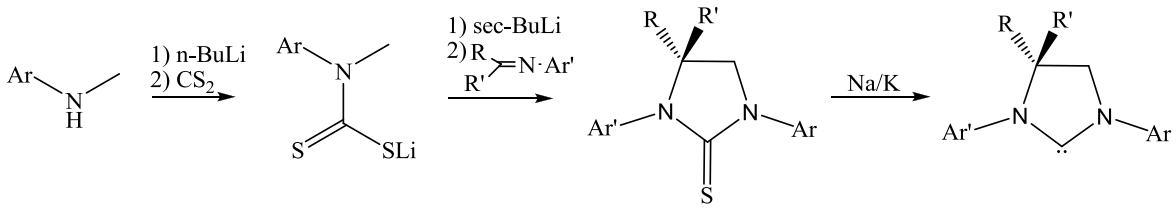
N-Heterocyclic carbene ligands with *syn* and *anti* methyl groups on the backbone were also reported and the catalytic performance of their ruthenium complexes has been evaluated towards metathesis reactions.[129]

Another interesting example of acyclic 1,2-diamine used for synthesis of imidazolinium salts is shown in Scheme 1.14.[130] Asymmetric induction of this and other NHCs derived from acyclic 1,2-diamines were tested for asymmetric synthesis of β-lactams.[131]



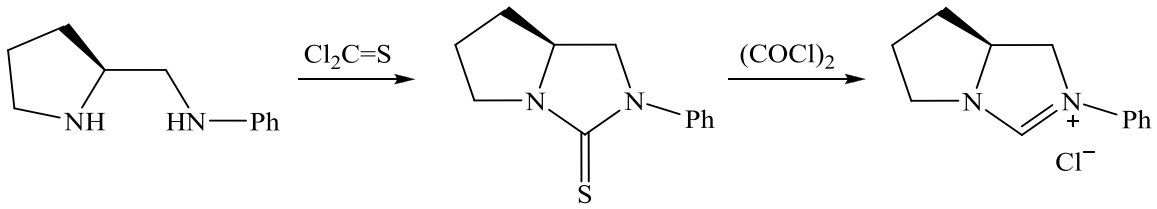
Scheme 1.14 Synthesis of imidazolinium salts from acyclic 1,2-diamine.

Using of enantiopure chiral diamines led to NHC ligands with chiral centers in C4 and C5 position but saturated carbenes that have only one stereogenic center in the backbone were also developed. First report regarding the synthesis of such imidazolinium salts was published in 2003 by Hahn et al.[132] who presented an easy synthetic approach to unsymmetrically substituted saturated NHC using secondary amines as starting material. The product was usually a racemate.



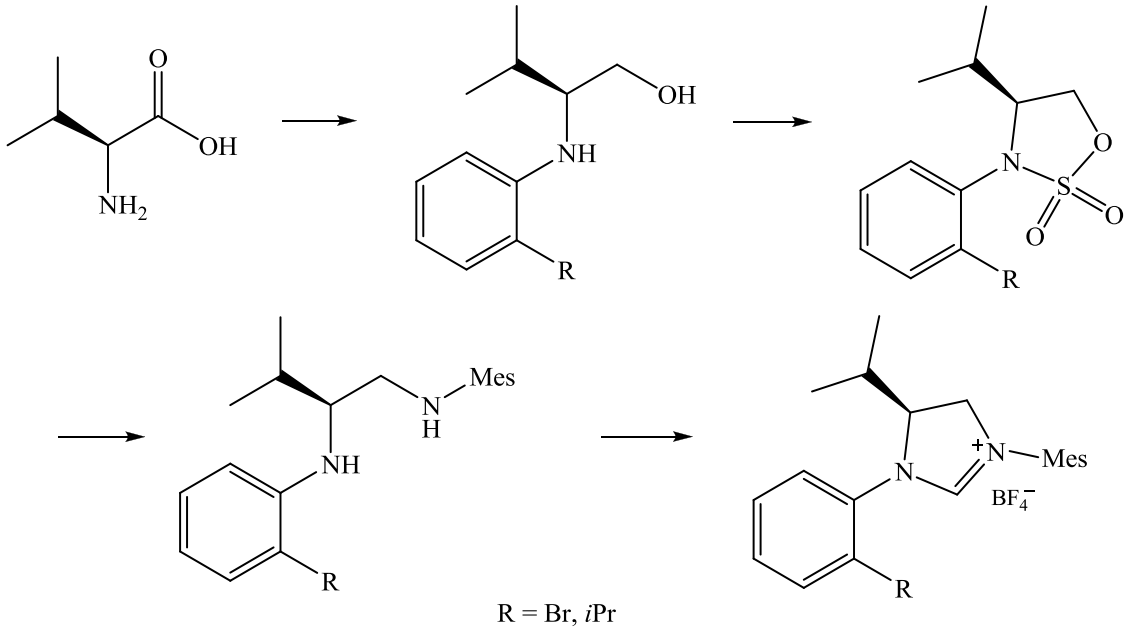
Scheme 1.15 Synthesis of chiral NHC with one asymmetric center in the backbone.

Synthesis utilizing an enantiomerically pure chiral diamine derived from L-proline, a naturally occurring amino acid was described later. The synthetic protocol is shown in Scheme 1.16. Its palladium complexes were tested for cross-coupling reactions.[133]



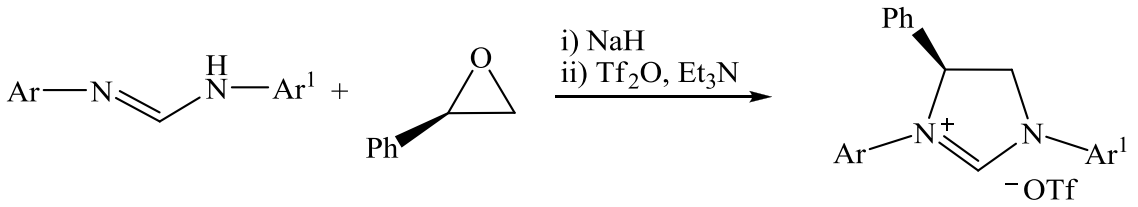
Scheme 1.16 Synthesis of imidazolinium chloride from a L-proline derived diamine.

Another amino acid, L-valine, was used as starting material for synthesis of chiral imidazolinium salts (Scheme 1.17) and theirs ruthenium complexes were tested for asymmetric metathesis reactions.[134]



Scheme 1.17 Synthesis of chiral imidazolinium salts starting from L-valine.

More straightforward access to backbone substituted chiral imidazolinium salts from the reaction of formamidines with (*R*)-styrene oxide was also presented and is shown below.[135]



Scheme 1.18 Synthesis of chiral imidazolinium salts from *N*-*N*'-diarylformamidines.

Combination of both endocyclic and exocyclic chirality within saturated NHC precursors is also possible using synthetic protocols showed previously. Two examples are shown below.

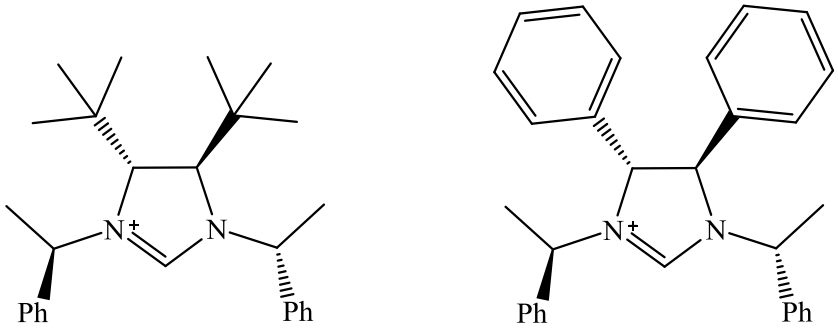


Fig. 1. 25 Imidazolinium salts with endocyclic and exocyclic chirality.

Imidazolinium salts possessing only exocyclic chirality have also been reported. Among them synthetic protocols for synthesis of salts containing planar chiral [2.2]paracyclophane,[69] chiral 2,5-dimethylpyrrolidine,[136] L-proline, L-phenylaniline,[137] carbohydrate,[138] chiral *ortho*-substituted α-alkylbenzylamines[139] moieties as *N*-substituents were described (Fig. 1.26 a-d). Chiral concave imidazolinium salts with axial chirality have also been developed.[140]

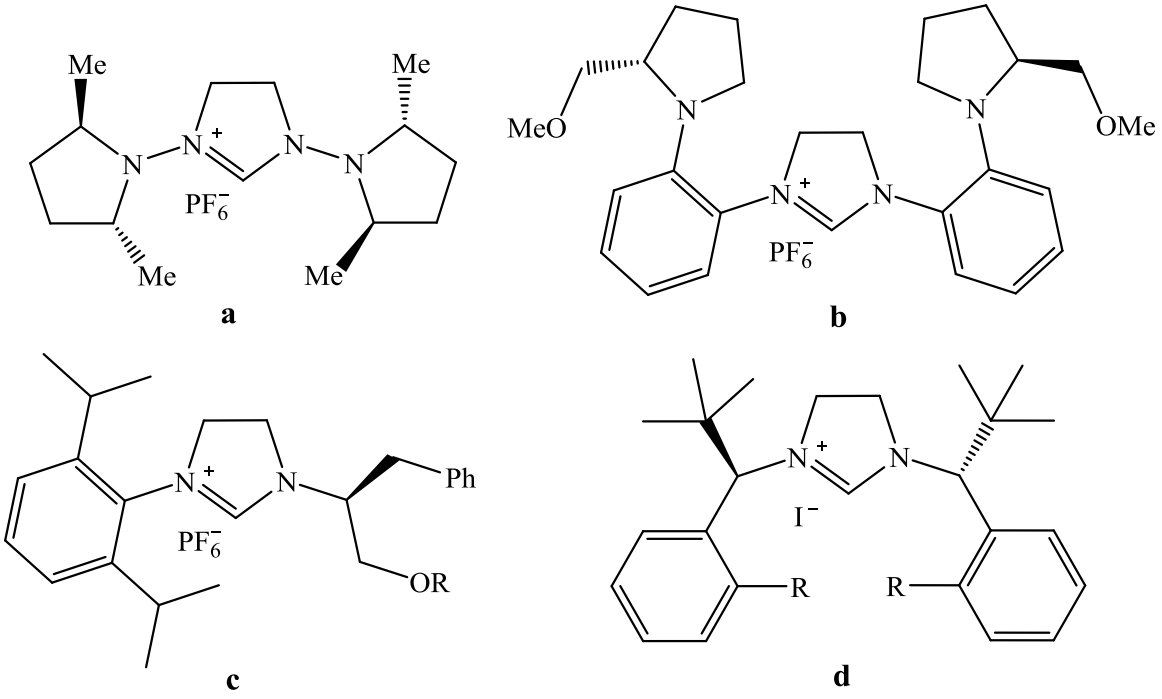


Fig. 1.26 Imidazolinium salts with chiral substituents derived from: a) pyrrolidine, b) L-proline, c) L-phenylalanine and d) *ortho*-substituted α-alkylbenzylamine moieties.

Chiral *N*-heterocyclic carbene ligand system can also be assembled using 2,2'-bipiperidine, biisoquinoline or 2,2'-bisquinoline templates.[65,141] Examples are shown below.

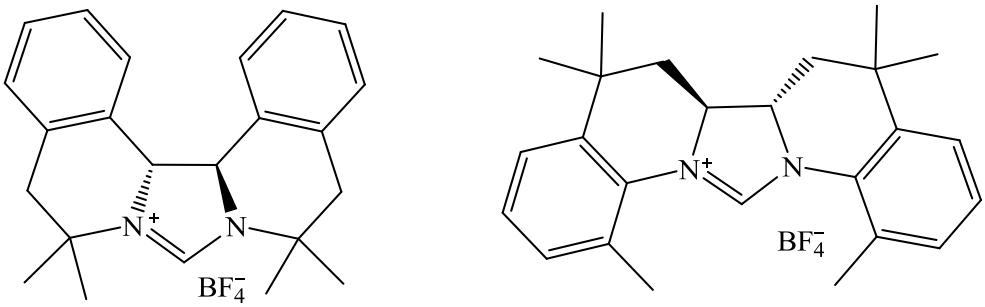


Fig. 1.27 Saturated NHCs with biisoquinoline and bisquinoline skeleton.

1.4.2.2 Bidentate imidazolinium salts

Further parallel investigation of the *N*-heterocyclic carbene field has resulted in the synthesis of chiral bidentate NHC ligands. Preference for a bidentate imidazolinylidene was based on the hypothesis that such a ligand would induce chirality more effectively than a monodentate ligand.[121a] In 2002 Hoveyda et al.[63,142] described chiral bidentate NHC precursor based on an symmetric aminohydroxybinaphtalene that was first used to form its chiral ruthenium complex for asymmetric olefin metathesis or efficient Cu-catalyzed enantioselective allylic alkylations. The same group use later the biphenyl scaffold that occurred to be sufficient for axial chirality and combined it with additional endocyclic chirality to obtain chiral Ag-based NHC complex.[143] They continued their research in this area and reported more recently sulfonate containing NHC ligands with stereogenic centers on C4 and/or C5 positions. They served as ligand for Ag-based complexes and were used and tested in Ru-catalyzed asymmetric metathesis reaction and Cu-catalyzed allylic alkylation for total synthesis of natural products.[144] Other chiral 4-substituted imidazolinium salts bearing sulfonates obtained from Boc-protected amino alkohols and theirs use in γ-selective reactions of allylic halides with Grignard reagents were described in 2012 by Simon Woodward.[145] The synthesis of enantiopure unsymmetrical *N*-heterocyclic based zwitterions incorporating imidazolinium and alkylsulfonate or sulfamate groups proved to be versatile chiral solvating agents was also reported.[146] Fig. 1.28 summarizes chiral imidazolinium salts described above.

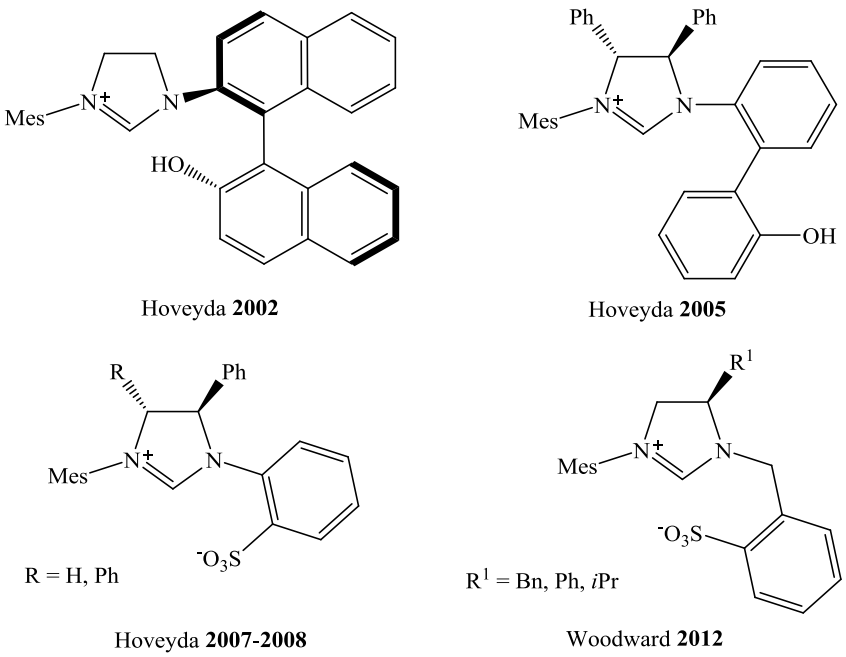
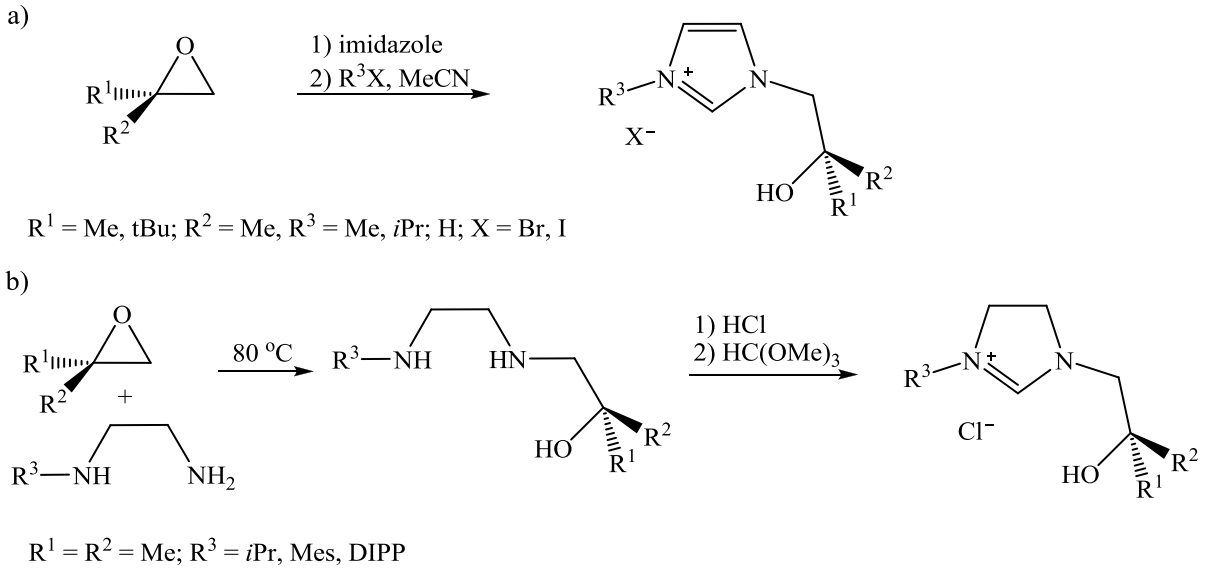


Fig. 1.28 Examples of chiral bidentate imidazolinium salts.

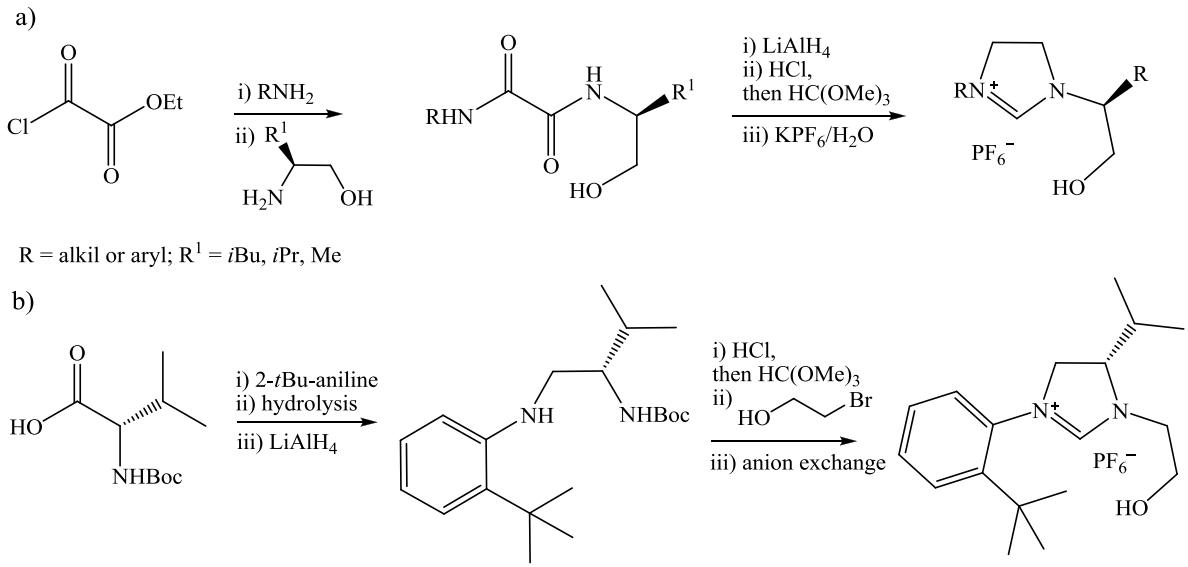
Arnold et al.[147] isolated and reported the first chiral chelating alkoxy-imidazolium salts obtained in an one-pot reaction of two equivalents of *N-tert*-butylimidazole with 2-chloromethyl-2-phenyloxirane in 2001 (Scheme 1.19 a). Seven years later they described the synthesis of their saturated analogues (Scheme 1.19 b). Protonolysis chemistry with yttrium and uranyl amido complexes have afforded the first early transition metal, and the first f-block saturated carbene complexes.[148]



Scheme 1.19 Synthesis of: a) chiral chelating alkoxy-imidazolium salts and b) its saturated analogue.

A series of chelating achiral NHC ligands that feature a chelating phenolic unit coordinated to Pd-complexes were described by Grubbs in 2004.[149] But yet the first synthesis of chiral alkoxy-imidazolinium salts that were derived from L-valine in a six step procedure were reported in 2004. These salts have been used as chiral derivatizing agents for *ee* determination of chiral carboxylate.[150] The same group decided to evaluate the potential of this salts as new chelating alkoxy-NHC ligands in the enantioselective Cu-conjugate addition of diethylzinc to cyclohexenone or Cu-catalyzed asymmetric conjugate addition of Grignard reagents to trisubstituted enones to form all-carbon quarternary chiral centers. They have extended this new class of imidazolinium salts through synthesis of 20 other salts derivatives easily accessible from commercially available *β*-aminoalcohols and various substituted anilines or alkylamines.[151] They continued research in the area of this class of imidazolinium salts tested in the above mentioned transformations and have more recently reported several additional alkoxy-chelating derivatives possessing the stereogenic center

in the heterocyclic ring or in chelating side chain starting from amino acids with various *N*-substituents.[152]



Scheme 1.20 Synthesis of alkoxy-imidazolinium salts with stereogenic center in a) chelating side chain or b) within the heterocycle.

Moreover simple chiral bidentate NHC ligands that carry an achiral coordinating group as *N*-substituent and possess two stereogenic centers within the heterocycle obtained in three-step procedure were described by Katsuki.[153] They serve as efficient chiral auxiliaries for the Cu-catalyzed asymmetric conjugate addition of dialkylzinc to acyclic enones.

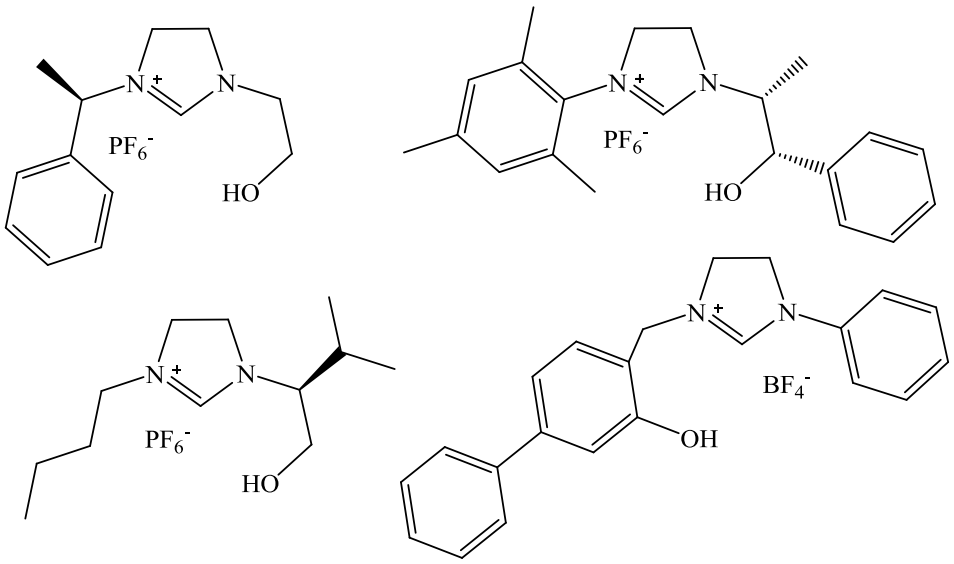
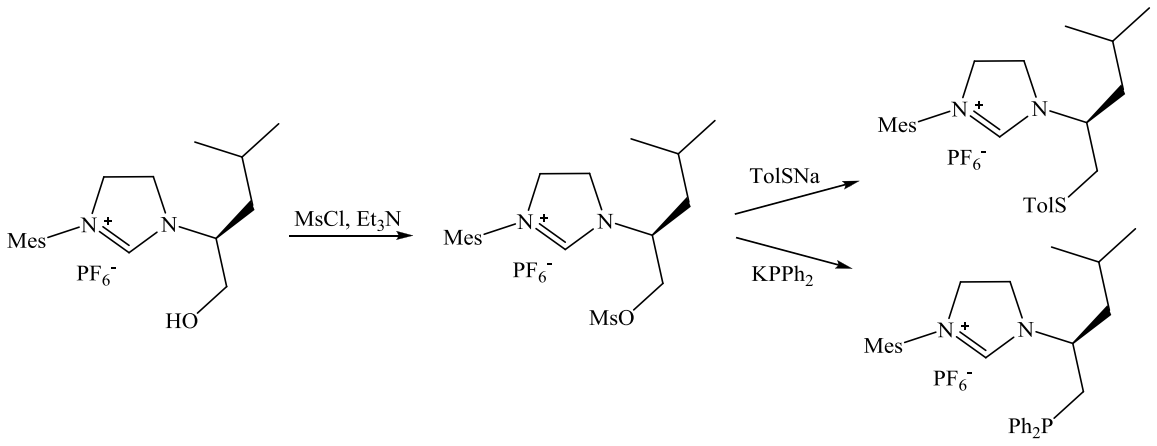


Fig. 1.29 Examples of alkoxy- and phenyloxy-imidazolinium salts.

The alkoxy bidentate NHC ligands are not the only example of this class of saturated NHC ligands. Phosphine-, thiolate-, mesylate-, tosylate- and picolyl-containing NHC ligands have also been reported. Mauduit`s group[154] introduced the second chelating function by converting the hydroxyl group into a leaving group such as tosylate and mesylate. Sulfur and phosphine function were introduced by nucleophilic substitution of the mesylate leaving group by using sodium thiolate and potassium diphenylphosphide, respectively (Scheme 1.21). These ligands have been evaluated in the enantioselective Cu-catalyzed conjugate addition to cyclic and acyclic enones displaying good catalytic activity.



Scheme 1.21 Synthesis of sulfur and phosphine functionalized NHCs.

Pfaltz et al.[155] on the other hand prepared phosphine- and phosphinooxy-substituted NHC ligands and theirs iridium complexes that were tested in Ir-catalyzed hydrogenation. Palladium complexes containing picolyl functionalized NHC ligands with different substituents were synthesized and tested for the Mizoroki-Heck reaction giving good conversion and regioselectivity.[156] Chiral bidentate NHC-thiolate ligands derived from levamisole were also reported. Their palladium complexes and triruthenium and triosmium carbonyl clusters were described.[157] Most recently chiral imidazolinium salts functionalized with urea-type hydrogen-bond donor moieties were prepared and their NHCs were evaluated as organocatalysts in enantioselective homoenolate additionreactions.[158] Examples of above mentioned NHC precursors are shown in Fig. 1.30.

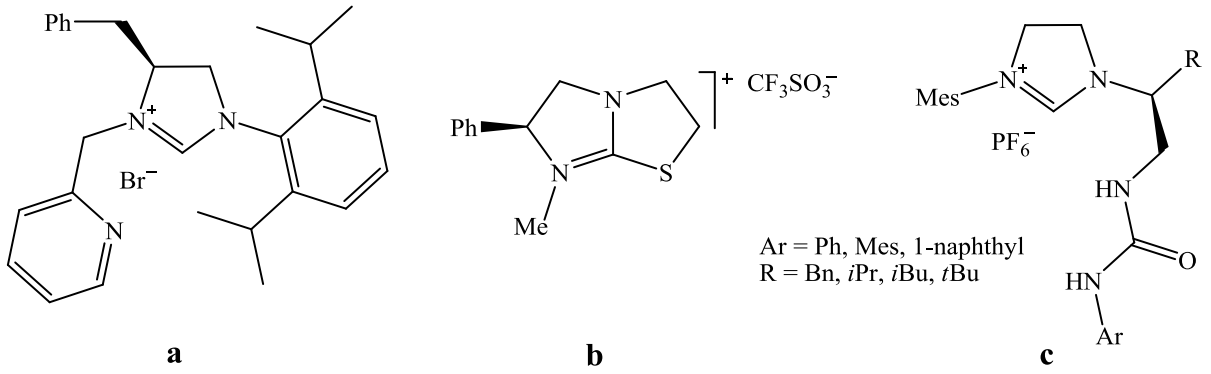
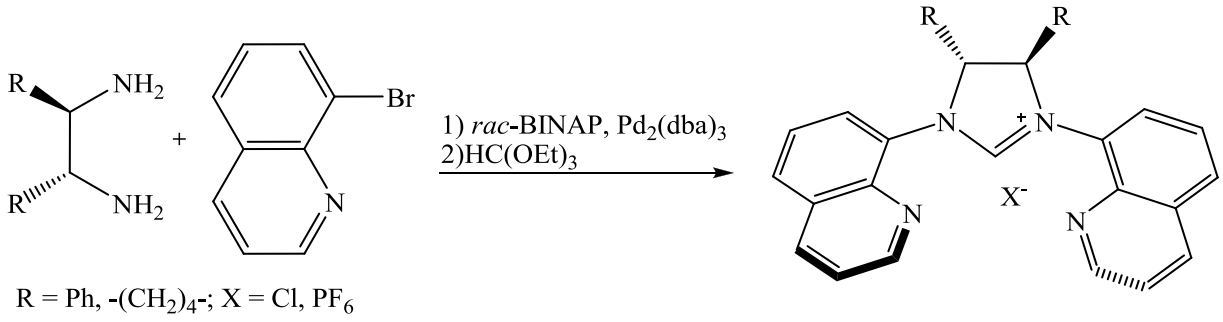


Fig. 1.30 NHC precursors with sulfur and nitrogen function: a) picolyl *N*-substituent, b) methyl levamisolium triflate, c) hydrogen-bond-donor-functionalized imidazolinium salt.

1.4.2.3 Tridentate imidazolinium salts

Angelici et al.[159] used (1*R*,2*R*)-diaminodiphenylethylenediamine and (1*R*,2*R*)-diaminocyclohehane as building block for first chiral tridentate diquinolyl-imidazolinium salt and its copper-complex (Scheme 1.22).



Scheme 1.22 Synthesis of diquinolyl-imidazolinium salt.

Simultanously imidazolinium salts incorporating two chiral hydroxy groups on their *N*-substituents were introduced by Wilhelm et al.[160] who prepared appropriate bis(amino alcohol) from amino alcohols and 1,2-dibromoethane or chiral diamines and then used triethyl orthoformate to close the ring. These ligands in combination with different metallic salts were investigated in the diethylzinc addition to aldehydes with good yields and enantioselectivity. Using similar procedure Zhengning et al.[161] synthesized imidazolinium salts containing two *N*-functionalized hydroxyl or alkoxyl groups that were applied to catalyze the asymmetric conjugate addition of diethylzinc to cyclohex-2-enone.

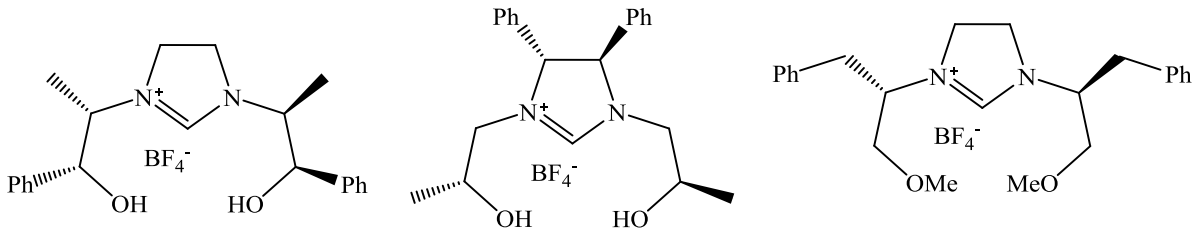


Fig. 1.31 Chiral symmetric NHC containing two *N*-functionalized hydroxyl or alkoxyl group.

The successful use of enantiomerically pure tridentate NHCs as chiral modifiers was reported in 2010.[162] Formation of a heterogeneous catalyst from Fe_2O_3/Pd nanoparticles and chiral tridentate imidazolinium salts enable creation of a catalytically active entities tested for asymmetric α-arylation reactions. Moreover this catalyst system is easy to remove and recycle without loss of activity and selectivity.

Part 2

2. Results and discussion

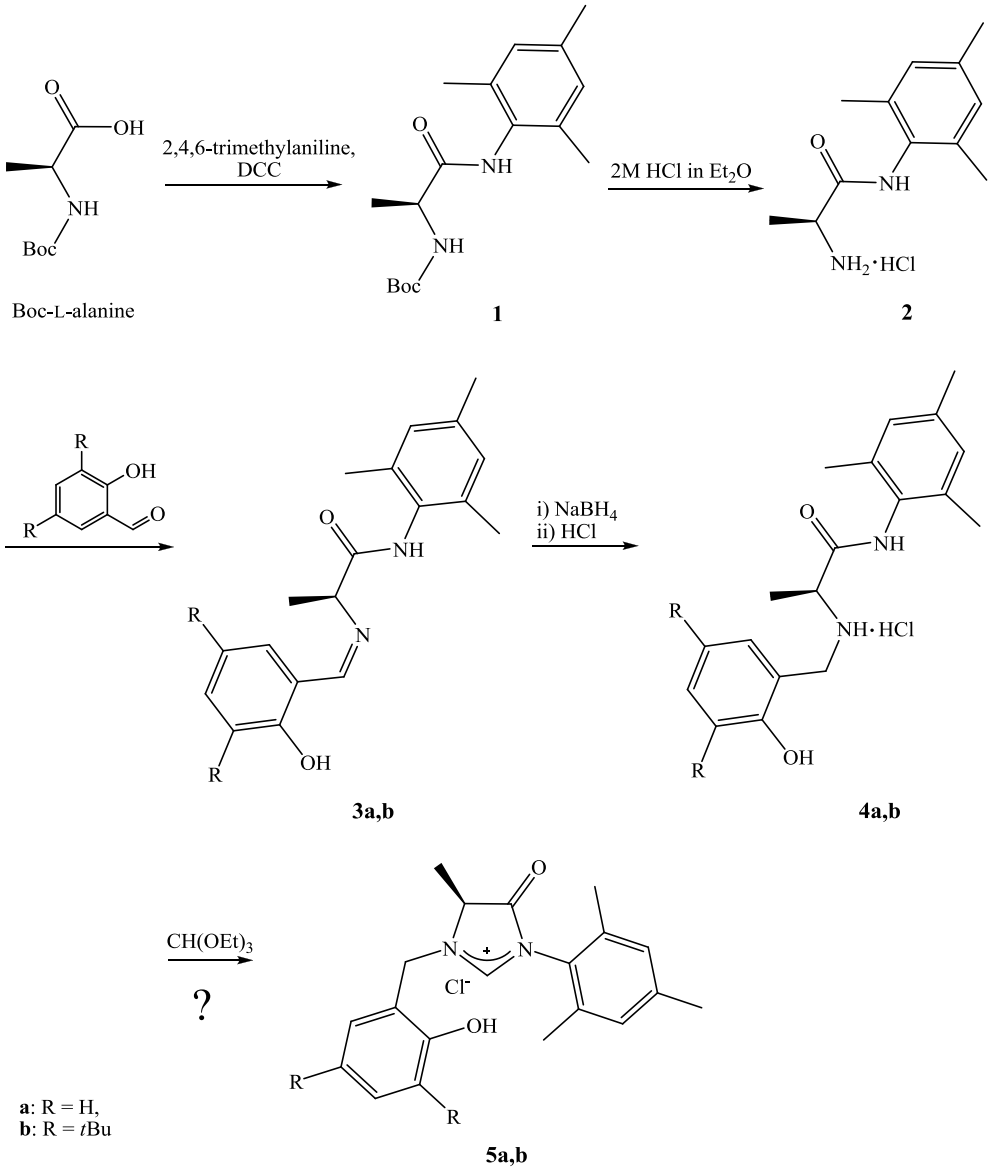
2.1 Introduction

Over the past two decades, great achievements were made in catalysis using NHCs as ligands. NHC ligands combined with metal pre-catalysts exhibit high activities in various important organic transformations including Pd-catalyzed cross-coupling reactions[163] and Ru-catalyzed metathesis reactions[164] or Rh-catalyzed hydrosilylation reactions[165]. A wide range of NHC ligands are now commercially available. The design of chiral NHCs for use in stereoselective catalytic transformations has been destined to provide an additional dimension to the field. Synthesis of new chiral NHC catalysts is supported by the development of new synthetic routes to chiral NHC ligands and their metal complexes.[41] Strategies have been explored that contain symmetrical or unsymmetrical, mono-, di- or tridentate NHCs with chirality within the backbone or on the *N*-substituents, which is described in the literature part of this work.

Considering, that even a minor change in the ligand sphere of the catalyst can significantly alter its stability, reactivity or selectivity, and thus enhance or reduce its efficiency, we developed in our group a new strategy of forming chiral, bidentate NHC ligands. Herein, we report the synthesis of chiral imidazolinium salts derived from commercially available enantiopure amino acids and attempts to obtain their late transition metal complexes.

2.2 Development of chiral, unsymmetrical imidazolylidene ligands starting from amino acids

The new synthetic route is proposed here to obtain chiral, bidentate imidazolinium salts that could serve as comfortable NHC ligands for late transition metal (Ru, Pd, Rh) complexes. The procedure for the synthesis of imidazolinium salts **5** as a five membered (amino)(amido) NHC ligand from enantiopure Boc-protected L-alanine as shown in Scheme 2.1 was initially attempted.



Scheme 2.1 The synthetic path for (amino)(amido)NHC precursors.

Treatment of Boc-protected L-alanine (the same procedure for D form) with 2,4,6-trimethylaniline in the presence of dicyclohexylcarbodiimide (DCC) in THF provided a product **1** in very good yield. Afterward the amine deprotection with 2M HCl solution in diethyl ether resulted in the 2-amino-*N*-mesitylpropanamide hydrochloride, **2**. Subsequent reaction with 2-hydroxybenzaldehyde or 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde in MeOH in the presence of MeONa led to Schiff bases **3a** and **3b**, respectively.

The compounds were identified by the ^{1}H NMR spectroscopy. Thus the formation of Schiff bases was confirmed by presence of -C*H*=N- resonances at δ=8.51 ppm for both; **3a** and **3b** derivatives (in $CDCl_3$). Overall yield after these 3 steps was 63%. Characteristic feature of all above mentioned derivatives in ^{1}H NMR spectra is the presence of resonance signals of the methyl group attached to the chiral carbon as a doublet at *ca* 1.6 ppm and a methine proton at the chiral carbon as a quartet at *ca* 4.2 ppm vicinally coupled with *J*~7 Hz.

Reduction of **3a** and **3b** with $NaBH_4$, followed by addition of HCl afforded (amino)(amido) hydrochloride derivatives **4a** and **4b**. Vicinally coupled resonances from the methyl group protons and hydrogen attached to the chiral carbon were observed at 1.7 ppm (doublet) and at 4.3 ppm (multiplet).

The last step, i.e. reaction of **4a** and **4b** with triethyl orthoformate that aimed at the corresponding imidazolinium chloride salts: **5a** and **5b** led after chromatographic workup into hydrolized species of the mass enlarged by one oxygen atom in comparison with that of **5a** as identified by mass spectrum (Fig. 2.1). After incorporation of carbon atom into **4a** at least three possible intermediates which can be formed (Scheme 2.2). Eventually, only two of them can lead to the final compound **6**.

The NMR spectra of **6** are composed of two sets of resonances. The mixture of products in the molar ratio 1.0 : 0.8 was repeatedly isolated from the reaction mixture. Its ^{1}H NMR spectrum in DMSO-d_6 is shown below (Fig. 2.2 c). There are 6 resonances in the region 8.2-9.9 ppm in the ^{1}H NMR spectrum in dmso-d_6 (Fig. 2.2 c). Four of those disappear upon addition of deuterium oxide in situ (Fig. 2.2 b). Upon addition of KOH to the starting compound the same resonances disappear and additionally all proton resonances shift remarkably upfield (Fig. 2.2 a).

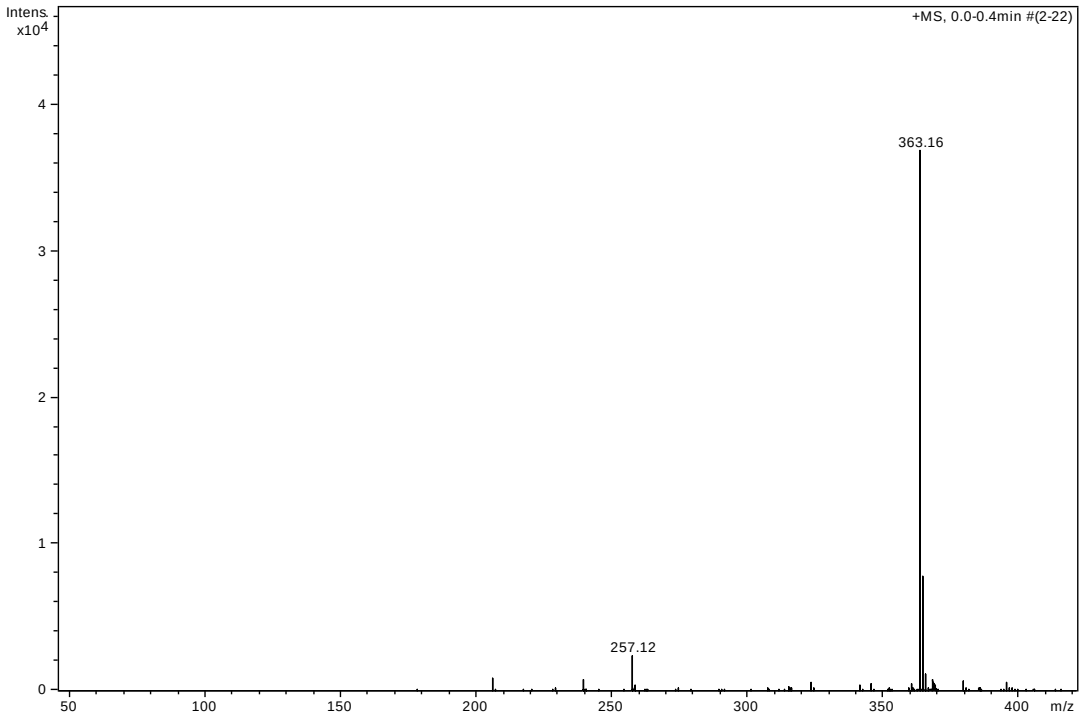
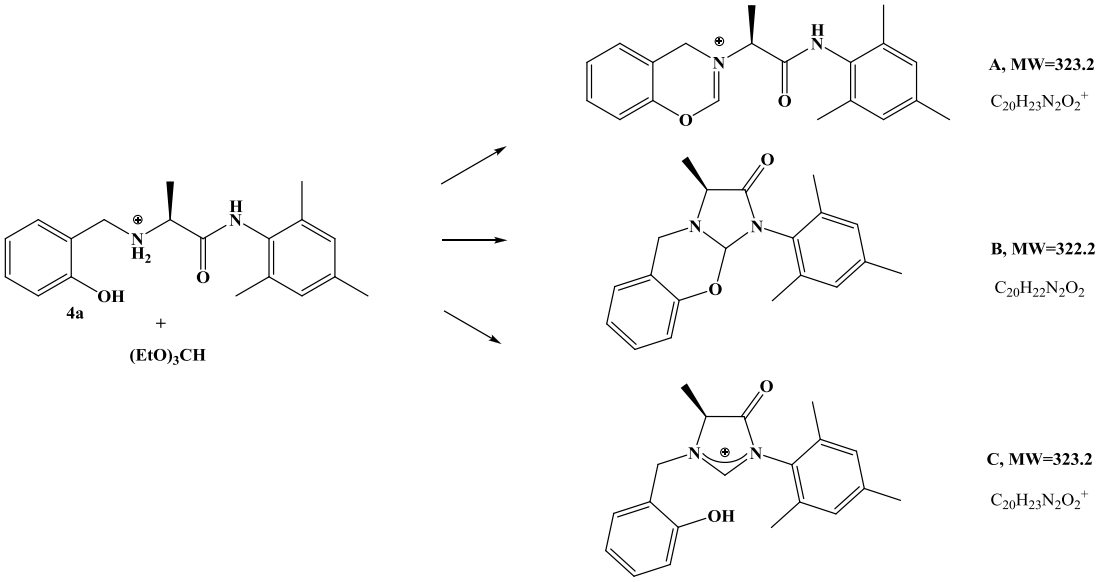


Figure 2.1 Mass spectrum of **6** - the product of ring closing reaction of **4a**.



Scheme 2.2. The possible products of reaction of **4a** with triethylortoformate.

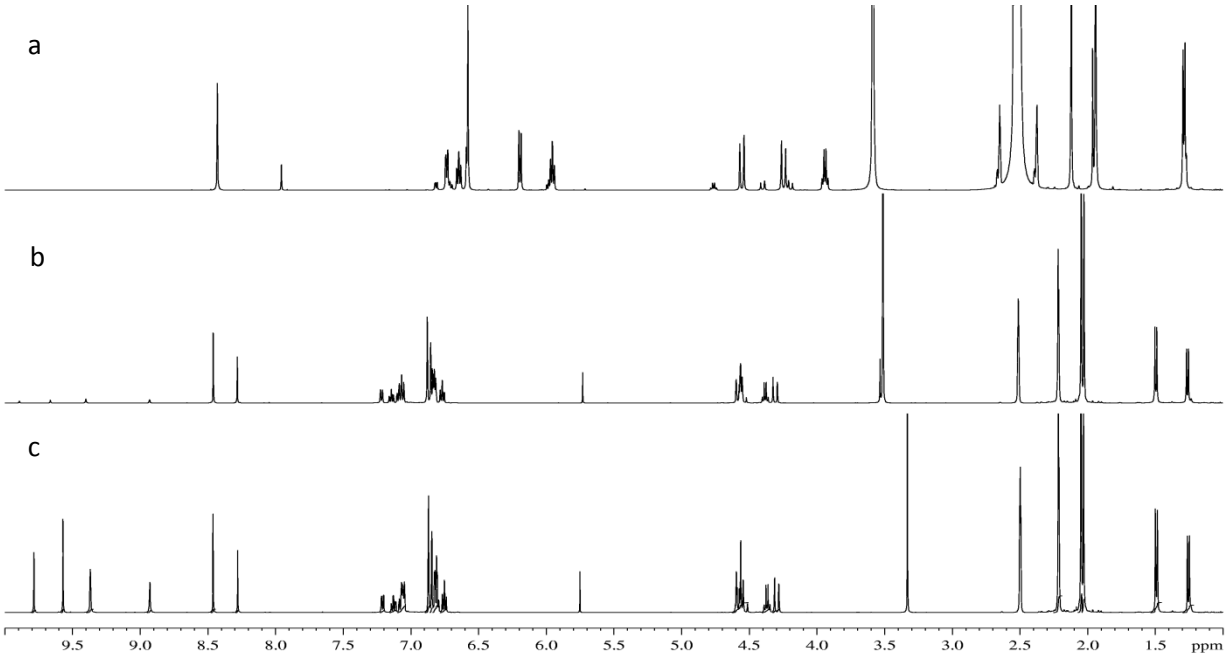


Figure 2.2 The ^{1}H NMR spectra in dmso-d_6 for a) mixture after addition of KOH in H_2O, b) mixture after addition of D_2O, c) mixture of two products **6**.

The spectral characteristic feature of imidazolidine salts, like **5**, is the presence of: -N-C*H*-N- proton resonance at ca 8-9 ppm and coupled resonances of CH_3- group and hydrogen attached to chiral carbon at ca 1.7 (doublet) and in the 3.5-4.5 region (quartet), respectively. The methylene diastereotopic protons of this moieties should give characteristic resonance signal pattern in ^{1}H NMR spectra as two separate doublets with geminal coupling constant, *J*~14 Hz.

Almost all of the proton and carbon resonances of **6** were doubled so that in both ^{1}H and ^{13}C NMR two sets of similar resonances were observed, what could indicate the presence of two isomers. Characteristic resonance signals in ^{1}H NMR around 8.2-8.5 ppm assigned to -N-C*H*-N- proton (initially considered as originated from imidazolidine moiety) were observed. Moreover characteristic resonance signals of diastereotopic methylene group proton resonances in the region 4.35-4.73 ppm occur as two pairs of dublets with coupling constant *J*=14 Hz and the methine proton of the chiral carbon at 4.27 ppm (second one at 4.85 ppm) coupled with methyl group protons at 1.65 (second one at 1.55 ppm) indicated the presence of -Ar-CH_2-N-CH(CH_3)-CO- fragment.

Two isomers remained at the same molar ratio in every synthetic attempt, suggesting the two compounds were rotational isomers. Therefore I have performed the variable-temperature ^{1}H NMR measurements of the mixture in DMSO-d_6. Fig. 2.3 demonstrates two relevant fragments of spectra (4.2-4.7 ppm and 2.4-1.1 ppm) recorded at 25 ºC, 45 ºC, 75 ºC, 100 ºC, 125 ºC, 150 ºC.

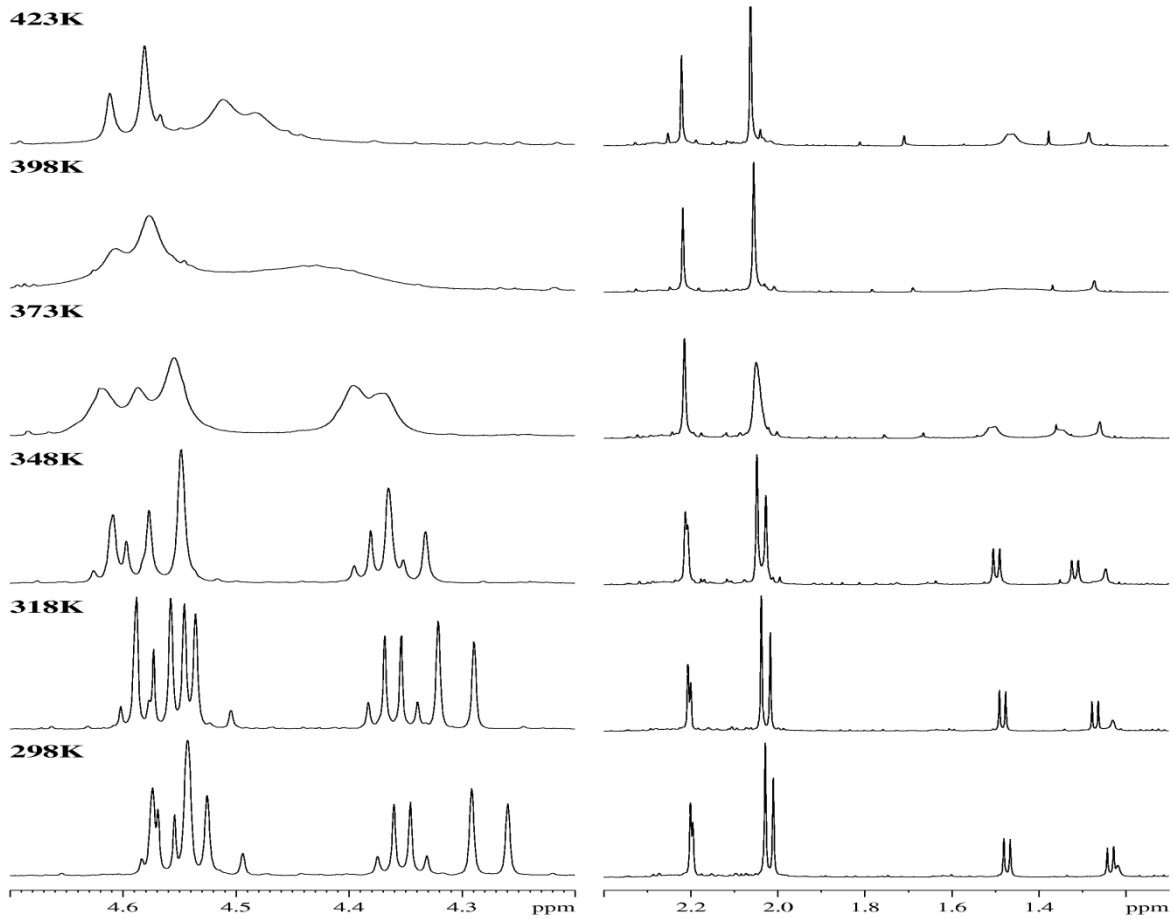
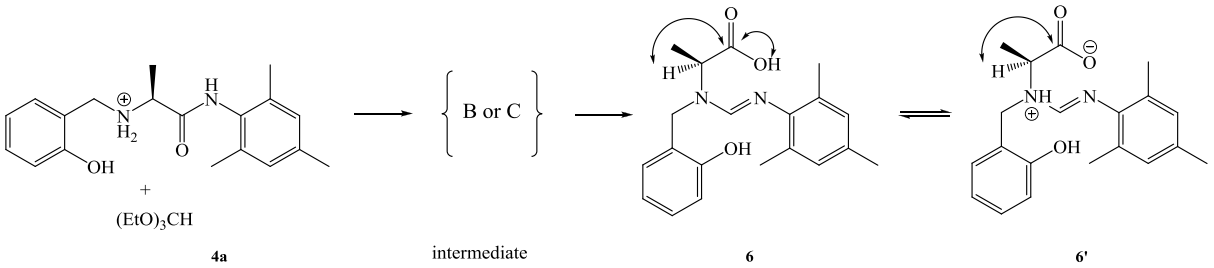


Fig. 2.3 Temperature dependent ^{1}H NMR spectra of mixture **6**:**6'** 1.0:0.8 in DMSO-d_6.

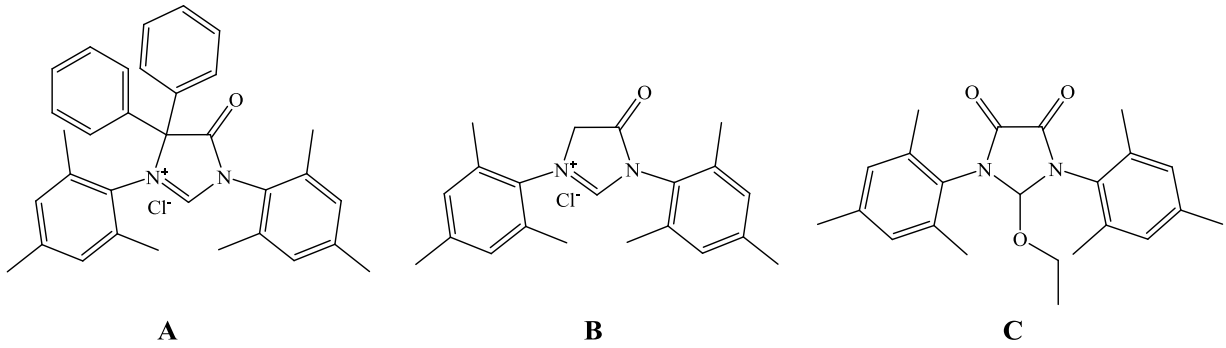
The coalescence point was observed at 373 K, indicating that **6** and **6'** are interexchangable isomers.

Considering the NMR spectra and final formula of the compounds **6** the probable route and structure of the product can be that showed at scheme 2.3. Thus, **6** can be considered as product of hydrolysis of unstable intermediates B or C (presented at scheme 2.2). Within this product **6**, the protonation-deprotonation intramolecular equilibrium probably takes place. Namely, the compound can be considered as zwitter-ionic tautomer, because the carboxyl group has pK_a *ca* 5, while aminidium group proton pK_a is much larger. Nonetheless, the cross-peak in HMBC spectrum indicates that even temporary attachment of this proton into carboxylic carbon takes place. The presence of two isomers, probably *cis-trans* around amidinium C=N bond might lead to doubled NMR spectra of **6**.



Scheme 2.3. The structure of side-product **6** on the basis of mass and NMR spectra. The arrows indicate the magnetization transfer from neighboring hydrogen into carboxylic carbon in HMBC experiment.

The attempts to obtain similar (amino)(amido)NHC ligands or bis(amido)NHC ligands were undertaken in our laboratory and described in the doctoral thesis of Allaert (Fig. 2.4).[166a] The NHC ligands were successfully obtained in case of NHC precursors **A** and **C** and failed or were not reproducible for the imidazolinium salt **B**. Only cationic ligand of **A** salt was introduced as carbene ligand into Ru complex.



A **B** **C**

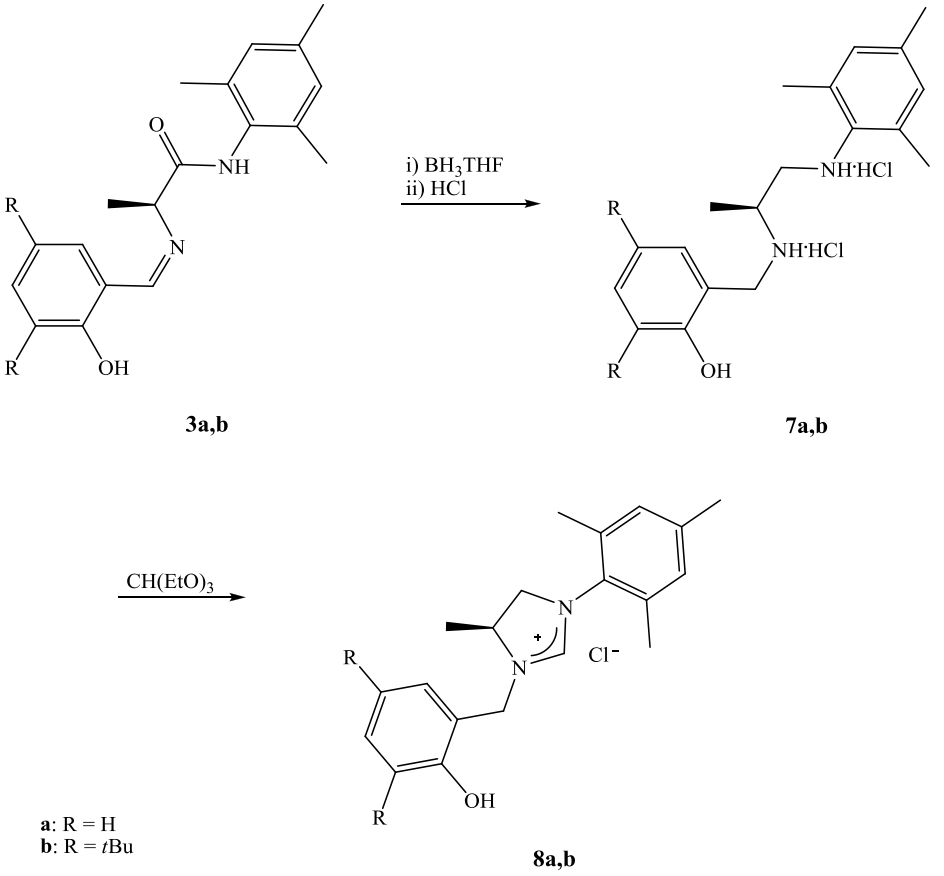
Fig. 2.4 (Amino)(amido)NHC precursors.

Presumably the difficulties in obtaining this class of NHC precursors or corresponding carbenes were caused by the presence of α-carbonyl protons in **B** or insufficient stabilization of the carbene through mesomere donation of the substituents.[166a]

Considering the starting enantiomerically pure alanine, the another issue which might lead to loss of chirality on α-carbon was enolization reaction in compound **5**, if isolated. The racemization might involve the enol form, which was in fact isolated and characterized by Benhamou et al for imidazole-2-ylidene-4-olate.[166b-c]

On the basis of above mentioned experiences and due to inconvenience of the last step of synthetic route presented at Scheme 2.1 I have modified the synthetic route to obtain NHC

ligands. I have replaced the selective reducing agent $NaBH_4$ with stronger BH_3·THF complex. That caused the reduction of both -C=O bond to $–CH_2$- and -CH=N- bond to -CH_2-NH- affording diamine hydrochlorides **7a** and **7b**. After reaction with triethyl ortoformate the desired imidazolinium salts **8a** and **8b** were obtained at good total yield (Scheme 2.4).



Scheme 2.4 Synthetic path of imidazolinium salts **8a** and **8b**.

Using this route four imidazolinium salts starting from Boc-L-alanine (**8a**, **8b**) and Boc-D-alanine (**8c**, **8d**), which formulae are shown in Fig. 2.5, were obtained.

Identity of the final imidazolinium salts were confirmed by NMR, IR, MS spectra and elementary analysis. The assignment of resonances of all obtained products in the ^1H and ^{13}C NMR spectra was performed using 1D and 2D homonuclear COSY and heteronuclear HSQC and HMBC experiments.

The expected feature of the ^1H NMR spectrum is related to the chiral imidazolydine carbon originated from enantiopure substrate: L- or D-alanine. Thus methylene protons of *N*-benzyl groups as well as those attached to imidazolydine carbon next to chiral center, should be diastereotopic, while the resonance of hydrogen attached to chiral carbon should be multiplet.

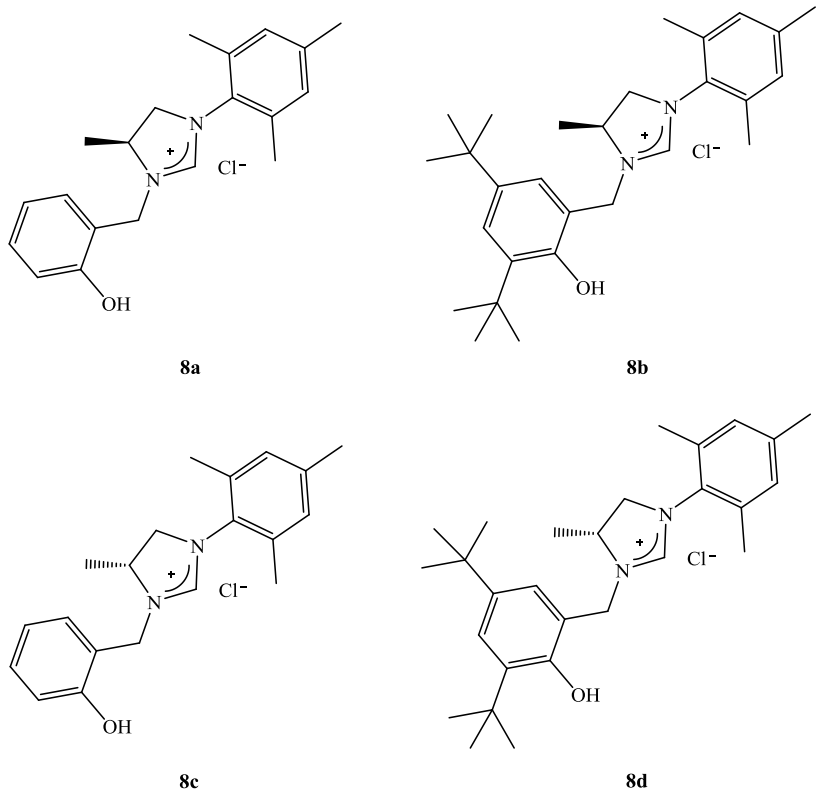
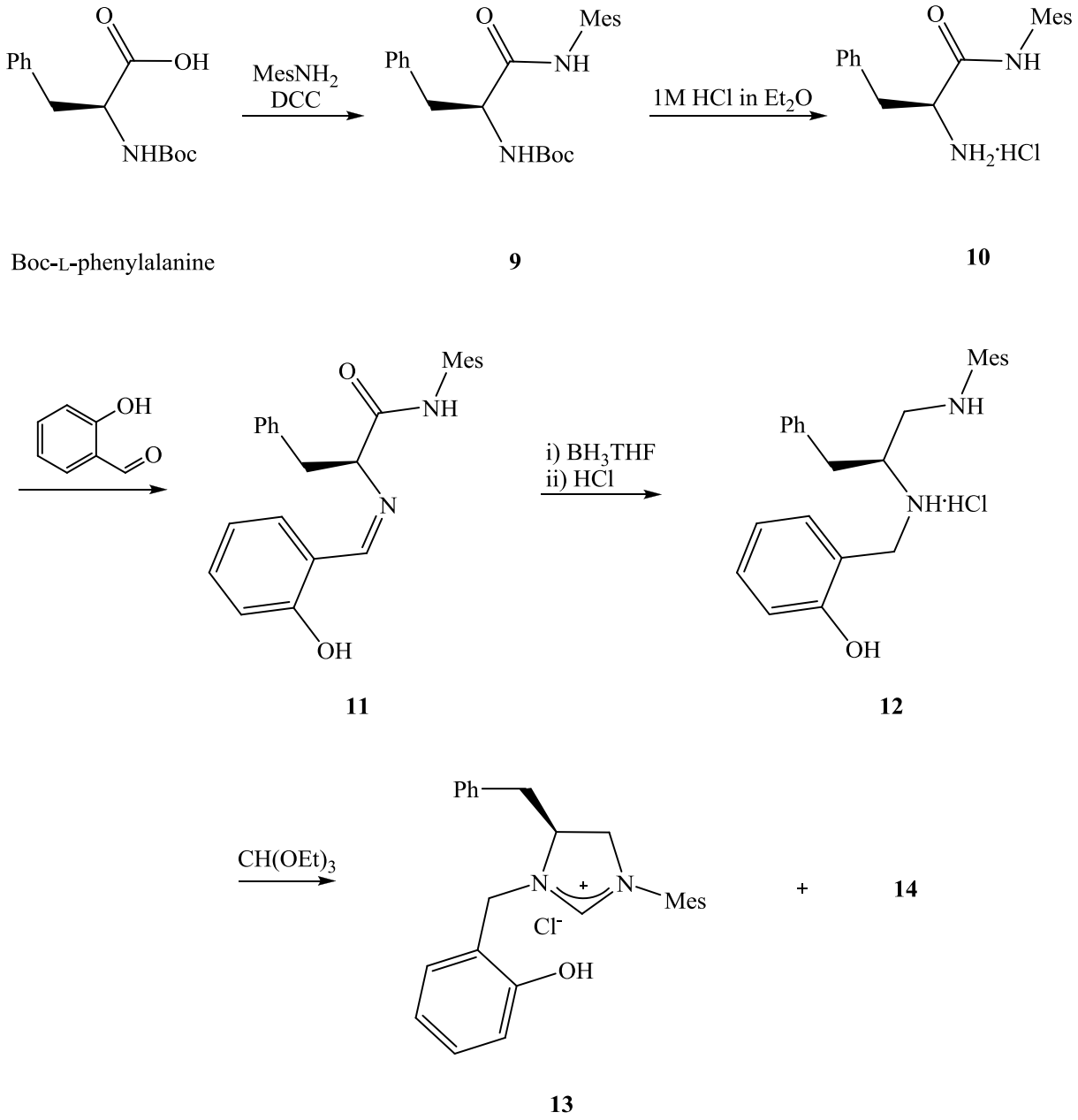


Fig. 2.5 Hydroxybenzyl imidazolinium salts obtained from enantiopure L- and D-Boc-alanine.

Indeed, the benzyl methylene protons show high magnetic non-equivalence; the chemical shift difference between them is 0.27 ppm in **8a** and **8c** and 0.35 ppm in **8b** and **8d** compounds, and they are geminally coupled with *J*=14 Hz. Even larger chemical shift difference between ring methylene protons was observed, which in all cases was larger than 0.50 ppm. This is obvious because they are vicinal to methyl group and hydrogen atom attached to center of chirality, while benzyl methylene hydrogen atoms are one bond further from substituents at chiral carbon. The diagnostic for imidazolydine ring in **8** is the singlet resonance of –N-C*H*=N- ring proton, which appears at 8.90-9.00 depending on *N*-substituent. The total ^{1}H and ^{13}C resonance assignment of salts **8a** and **8b** shown in Fig. 2.5, is collected in Table 3.1 in the experimental part. The ^{1}H NMR spectra of salts **8** are slightly concentration dependent presumably due to dissociation of salts **8**. Thus, the spectra of **8a** and **8c** which were recorded at different concentrations, showed distinct chemical shifts. In order to confirm, that compounds **8a** and **8c** are indeed the enantiomers, the additional ^{1}H NMR experiment has been performed; the spectra of separate solutions of **8a** and **8c** were recorded, and then these solutions were mixed and the ^{1}H NMR spectrum was recorded. The spectrum of equimolar mixture of **8a** and **8c** was composed of one set of resonances.

Using analogue procedure I have prepared the imidazolinium salt starting from Boc-L-phenylalanine (Scheme 2.5). Products **9**, **10**, **11** were obtained using above described procedure and isolated at good yield. Directly after reduction of product **11** with BH_3·THF complex that afforded hydrochloride **12**, the reaction with triethyl ortoformate was performed to obtain ring closed product **13** with moderate yield. Its identity was confirmed by NMR and MS analysis. Hydrochloride **12** was not isolated from reaction mixture.



Scheme 2.5 Synthetic approach of product **13**.

Similarly the benzyl methylene protons show high magnetic non-equivalence; the chemical shift difference between them is 0.28 ppm and they are geminally coupled with *J*=14.5 Hz. Even a higher chemical shift difference between ring methylene protons was observed and equal to 0.41 ppm. On the other hand the shift difference between benzyl methylene protons attached to center of chirality was barely 0.06 ppm. The diagnostic for imidazolydine ring in **13** is the singlet resonance of –N-C*H*=N- ring proton, which appears at 8.97 ppm. The total ^{1}H and ^{13}C resonance assignment of salt **13** shown in Scheme 2.4 is collected in Table 3.1 in the experimental section.

As by-product imidazolinium salt **14** was isolated from the reaction mixture. However its mass and NMR spectra did not allow to conclude about its identity.

Because the problem of enolization on carbon-4 during the reduction step executed with BH_3, step **3** $\rightarrow$ **7** (Scheme 2.3), remained real danger to preserve enantiomeric purity in final products **8** and **13**, the final products $\mathbf{8_{a\text{-}d}}$ were checked by polarimetry or CD spectroscopy. I have found that pair of **8b** and **8d** compounds showed opposite specific rotation of -1.1 ± 0.1 and +1.3 ± 0.1{$[\alpha_D^{20}] = -1.1\ (2,\ MeOH), [\alpha_D^{20}] = +1.3\ (2, MeOH)$}. Although the specific rotation of **8a** and **8c** was too low to measure by polarimeter, the CD spectrum of **8a** showed, that compound was not racemate; two Cotton effects: the positive at 280 nm (+0.6) and negative at 255 nm (-0.25) were observed. For compound **13**, derived from L-phenylalanine, the specific rotation was much larger than for all compounds **8**, namely $[\alpha]_D^{20}$ = + 44.7.

With salts **8** and **13** in hand I decided to coordinate them to Ru-, Rh- and Pd-complexes to examine theirs behavior and utility as auxiliary ligands for this late transition metals. We thought they could serve as a useful chiral bidentate NHC ligands for metathesis reactions or C-C or C-N coupling reactions.

2.3 Synthesis of metal complexes

Transition metal complexes of NHC can be obtained using four methods:

a) reaction of a transition metal complex with a free carbene ligand that is preformed or generated in situ,
b) reaction of an imidazolium salt with a transition metal complex containing a basic ligand, like alcoholates,

c) transmetallation from a Ag-NHC complex,

d) reaction of an azolium salt with transition metal salt in the presence of a weak base.

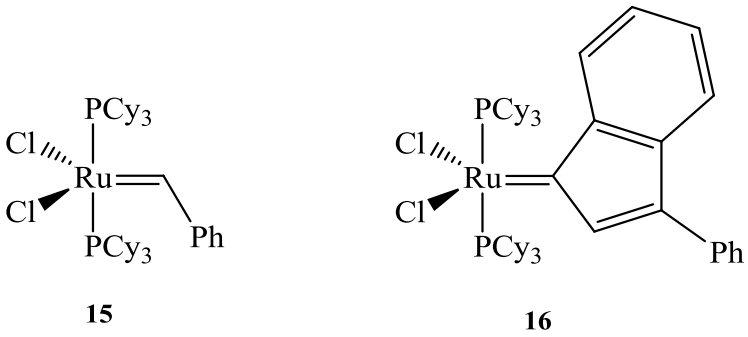
I have tested methods a and b in order to coordinate imidazolinium salt **8a** or carbene derived from **8a** to selected Ru, Rh and Pd complexes what will be further described.

2.3.1 Coordination of 8a to ruthenium(II)

The NHC-Ru complexes are known as useful and efficient metathesis reaction catalysts.[164,167]

Imidazolydinium cations undergo readily deprotonation upon various agents, like sodium hydride, alcoholates, or LiHMDS to generate carbene. The latter coordinates to ruthenium. Many Ru-NHC complexes are known, including those containing chiral NHC. Such ligands provide a chiral environment around the metal center and therefore might be useful to induce enantioselectivity in catalyzed reactions.[164] For synthetic purposes it seemed convenient to use ruthenium-phosphine complexes, because bulky phosphine ligands like tris(cyclohexylphosphine) (PCy_3) or triphenylphosphine (PPh_3) serve as readily leaving ligands.

I aimed at obtaining the ternary ruthenium complexes containing two carbon coordinated ligands. Bis(tricyclohexylphosphine)benzylidine ruthenium(II) dichloride (1st generation Grubbs catalyst, **15**) and bis(tricyclohexylphosphine)-3-phenyl-1*H*-inden-1-ylideneruthenium(II) dichloride (Neolyst (M1), **16**) were used as starting ruthenium substrate.[168] I considered that such complexes could serve as useful metathesis reaction catalyst and they will complement this big Ru-NHC complexes family.



15 **16**

Fig. 2.6 Ru-complexes used as starting materials.

At first I have decided to perform the reaction of **8a** and **15** in presence of strong base KHMDS in toluene in a NMR tube with external lock with $CDCl_3$ and I monitored the progress of reaction using ^{31}P NMR measurements. The spectra recorded after 1, 2, 4, 6, and 22 hours are shown in Fig. 2.9 below. After first few hours, resonance signal of complex **15** at 37 ppm was decreasing and resonance signal of tricyclohexylphosphine (PCy_3) at 11 ppm was increasing. This could indicate that phosphine ligand is leaving and exchanged by in situ generated carbene. After 22 hours complex **15** was completely consumed whereas at 46 ppm resonance signal of new complex containing at least one PCy_3 group was observed.

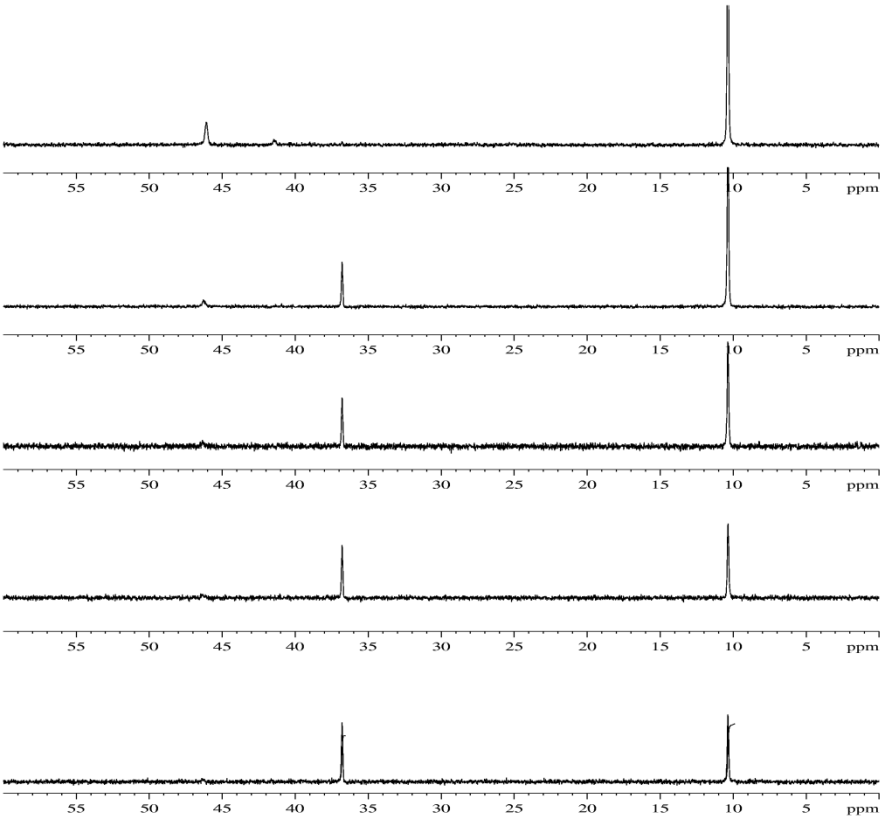
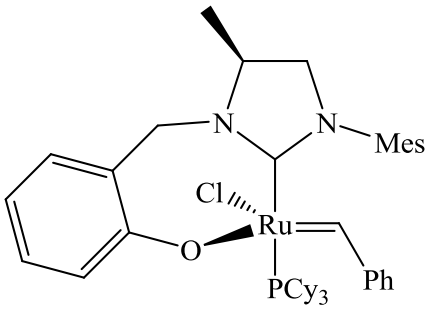


Fig. 2.7 ^{31}P NMR spectra of reaction of **8a** and **15** with KHMDS in toluene with $CDCl_3$ as external standard after 1, 2, 4, 6 and 22 hours (from bottom to top, respectively).

Careful examination of reaction mixture, which showed the presence of new weak intensity resonance signal in ^{31}P NMR suggested the formation of an intermediate form containing PCy_3 moiety in ternary Ru complex **17**.



17

Fig. 2.8 Probable structures of complex.

The same experiment was performed using **8b** as auxiliary ligand. Similar results were observed and the new ^{31}P NMR resonance signal from a new complex appeared at 47 ppm. However intensity of this signal was very weak.

The reaction of **8a** and **15** with KHMDS at the same conditions was monitored by ^{31}P NMR in $CDCl_3$ and resulting spectra are shown in Fig. 2.11 below. The resonance signal of starting product **15** was observed at 36 ppm and the resonance signal of free PCy_3 was observed at 11 ppm likewise in experiment shown above (Fig. 2.9) but any new signal was observed at ~46 ppm. Strong resonance signal assigned to tricyclohexylphosphine oxide (PCy_3O) at 51 ppm was observed instead. Since the first experiment was performed in NMR tube without protection against air and moisture and in the second experiment samples were taken, dried and redissolved in $CDCl_3$. Most probably only the complex **17** was formed and the intermediate form was not observed.

Encouraged by NMR sample scale experiments I tried to isolate product **17** from the reaction mixture. The first attempts gave promising result and I were able to isolate product containing NHC moiety. Presence of resonance signals between 4.7 and 3.2 ppm, characteristic for ligands **8** moiety, that were shifted in comparison with those of starting ligand **8a** in the same conditions, indicated the formation of a new product (this spectrum is shown in Fig. 2.10). Upfield coordination shift ~0.40 ppm for the diastereotopic methylene protons of *N*-benzyl groups as well as those attached to imidazolydine carbon next to chiral center and methine proton at chiral center were striking. But the lack of characteristic downfield signal at ca 19 ppm from the Ru=CH-Ph proton in ^{1}H NMR and ambiguous resonances in the aromatic region evidenced that the benzylidene moiety was missing in the product. In the ^{31}P NMR spectrum only single resonance signal at 51 ppm from the PCy_3O was observed. The obtained

quantity of product was insufficient for a full analysis and all further attempts to reproduce this reaction performed in the same conditions failed.

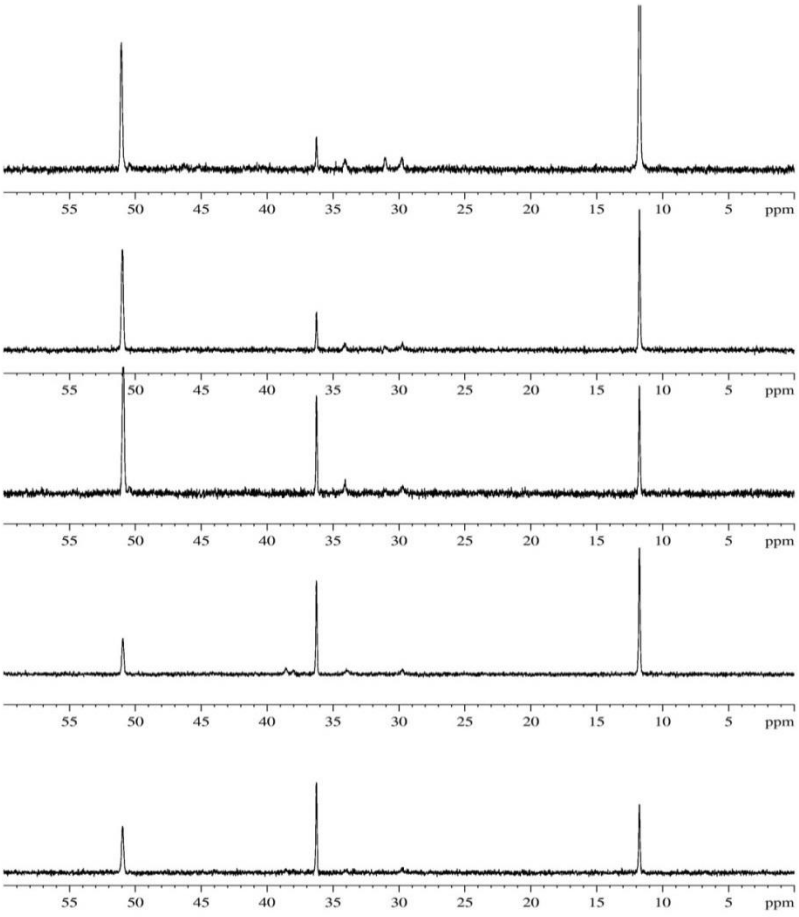


Fig. 2.9 ^{31}P NMR spectra of reaction of **8a** and **15** with KHMDS in $CDCl_3$ after 1, 2, 4, 6 and 22 hours (from bottom to top, respectively).

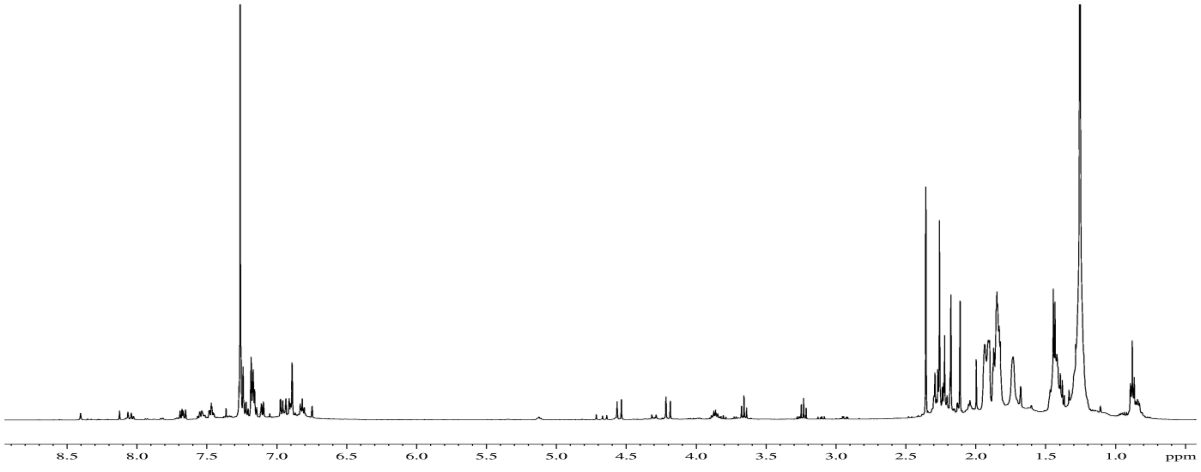
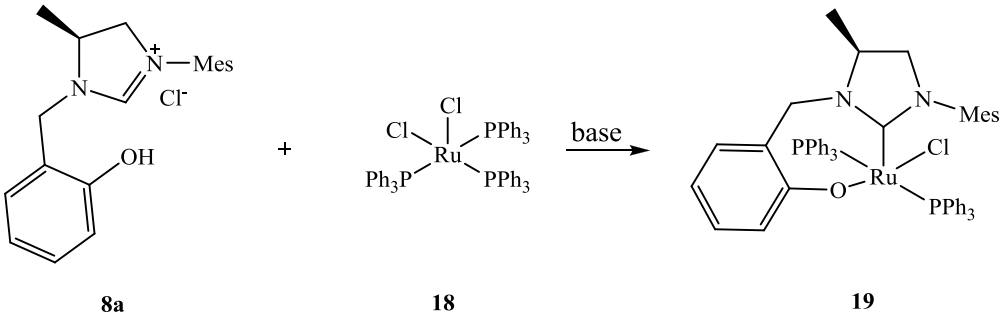


Fig. 2.10 The ^{1}H NMR spectrum of product isolated from reaction of **8a** with **15** in $CDCl_3$.

Therefore, I have changed the starting material to a relatively cheaper $RuCl_2(PPh_3)_3$ (**18**) complex in order to check if ligand **8a** would coordinate and isolation of its probable product (shown in Scheme 2.6) would be successful.



8a **18** **19**

Scheme 2.6 Coordination of ligand **8a** to Ru-complex **18**.

I have performed the series of experiments using THF or toluene as solvents and different bases such us: KHMDS, *t*BuOK, NaH, K_2CO_3. Coordination of ligand **8a** with complex **18** in presence of KHMDS or NaH did not occur. Purification of the reaction mixtures using flash column chromatography or crystallization did not allow to separate any of expected products.

The reaction of **8a** with complex **18** in the presence of *t*BuOK or K_2CO_3 in the 1:1:2 molar ratio in THF led to a mixture of new products. Presence of characteristic resonance signals from ligand **8a** in the ^1H NMR spectra and appearance of new resonance signals in ^{31}P NMR spectra indicated formation of new Ru-NHC complexes. On Figure 2.11 ^{31}P NMR spectra of isolated mixtures are compared.

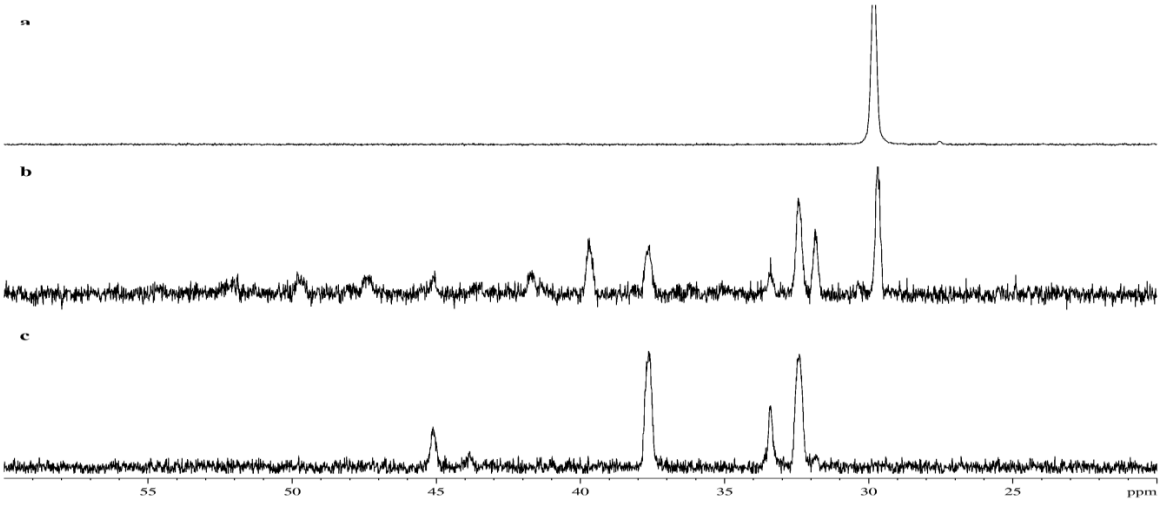
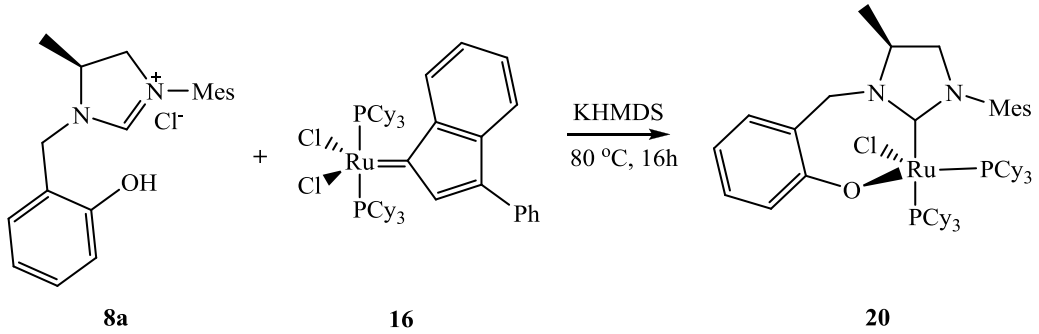


Fig. 2.11 ^{31}P NMR spectra of: a) starting complex **18** and products isolated in reaction with b) *t*BuOK and c) K_2CO_3. Spectra taken in $CDCl_3$.

Several new resonance signals were observed in both cases what could indicate formation of complex **19**, with various geometry **(**at least 3 isomers can be expected). However chromatographic separation of this mixture failed. Additionally all obtained and analyzed samples were contaminated both with free triphenylphosphine (PPh_3) and triphenylphosphine oxide (PPh_3O). Their resonance signal are observed in ^{31}P NMR spectra at -4 and 29 ppm respectively. This two resonance signals alone were observed in all samples received from reaction of **8a** and complex **18** with KHMDS and NaH. Probably the failure of previously described experiments was mostly caused by using the unstable starting materials, complex **18**.

Simultaneously, I tried to coordinate ligand **8a** to a Ru-indenylidene complex **16** that is more stable and less moisture and air sensitive. Taking into account my earlier experiments and after a few preliminary experiments with various solvents and bases I have performed the reaction according to Scheme 2.7 and identified product **20** as follows. The 1M KHMDS solution in toluene was used as a base. The workup of the post-reaction mixture by column chromatography the first, dark red fraction was isolated. The ^{1}H NMR spectrum of this crude fraction evidenced the presence of PCy_3 moiety and **8a** ligand (Figure 1.12 c). On the other hand the lack of resonance signals of the indenylidene moiety in the aromatic region of the ^{1}H NMR (for the spectrum of starting complex **16** see Fig. 1.12 b) suggested formation of imidazolinium Ru-complex **20** without indenylidene moiety in its structure. The spectrum of coordinated ligand **8a** showed no presence of N-C*H*-N resonance at 9 ppm, while all other resonances were shifted upfield if compare to that of free ligand (Fig. 1.12 a). Upfield coordination shift of ~0.40 ppm for the diastereotopic methylene protons of *N*-benzyl groups as well as those attached to imidazolydine carbon next to chiral center and methine proton at chiral center were observed.

The isolated product showed also the new resonance in the ^{31}P NMR spectrum, which did not originate from starting complex **16**, nor PCy_3 (Fig. 2.13).



8a **16** **20**

Scheme 2.7 The reaction scheme and isolated product **20**.

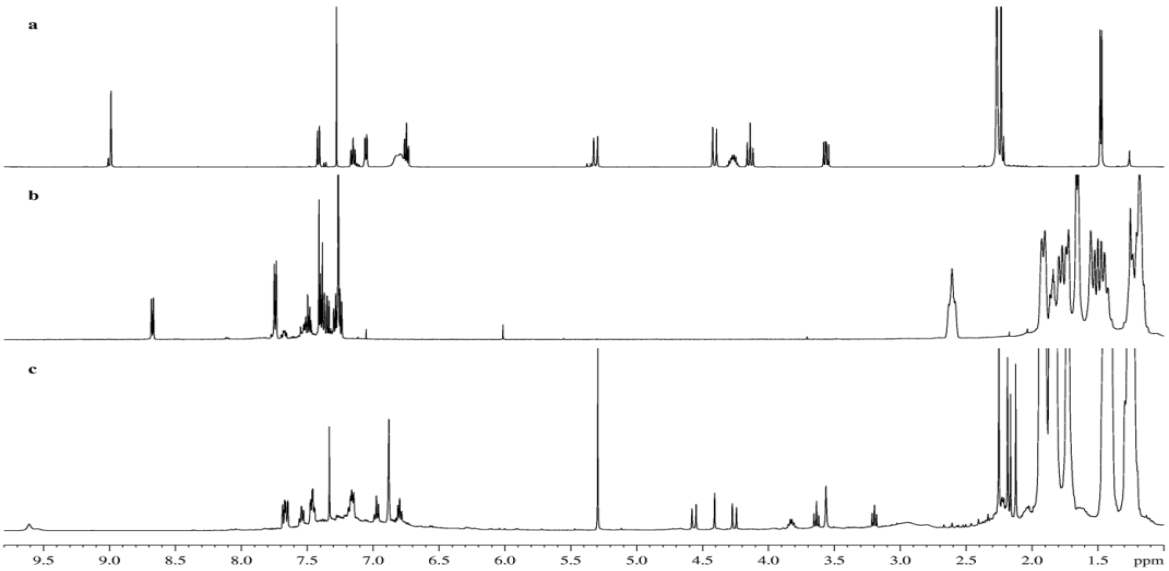


Fig. 2.14 The ^{1}H NMR spectra of: a) ligand **8a**, b) Ru-complex **16** and c) isolated product **20**, performed in $CDCl_3$.

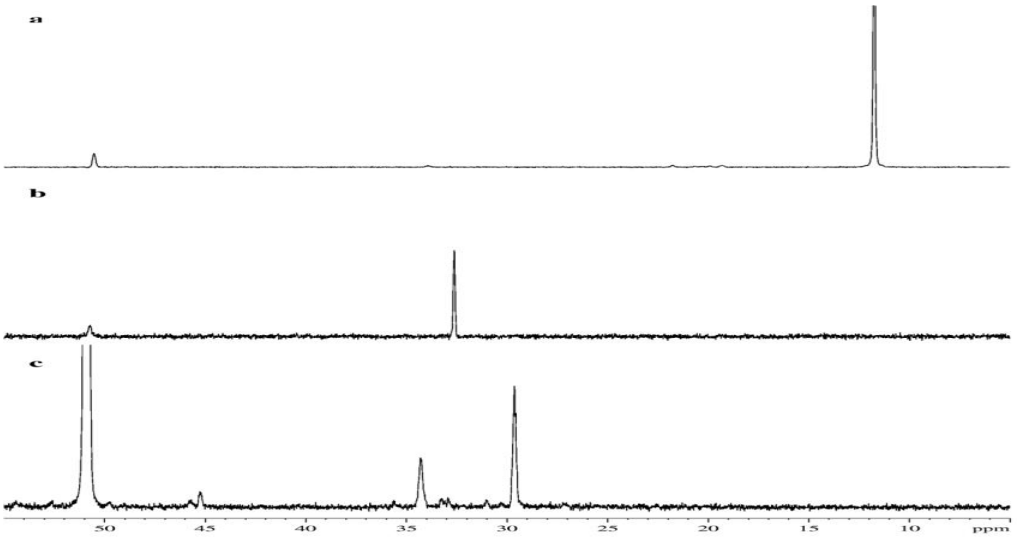


Fig. 2.13 ^{31}P NMR spectra of: a) PCy_3, b) Ru-complex **16** and c) isolated product **20**, performed in $CDCl_3$. The resonance signal at 51 ppm belongs to PCy_3O moiety.

Similar procedure was applied again to obtain the complex with two ligands: **8a** and indenylidene attached to ruthenium(II). The ligand **8a** was added to starting complex **16** and KHMDS as 1:1:10 molar ratio mixture was kept at room temperature for 36 hours to avoid decomposition of target product by dissociation of any ligands except chloride or phosphine.

Such a mild reaction conditions and separation by flash column chromatography resulted in isolation of the dark-red product, which showed quite complicated ^{1}H NMR spectrum (Fig. 2.14 c).

For comparison the ^{1}H NMR spectra of the mixture, probable complex **21** and starting Ru-complex **16** are shown in Fig. 2.14 (for clarity the range of $-PCy_3$ resonances between 2.0-1.0 ppm are omitted). This mixture was also subjected for MS spectrum, which showed the presence of two compounds numbered here as **21**. (Fig. 2.15).

In fact the mass spectrum is quite clear and indicates that two compounds are: [(**8a**-H)$_2$Ru(Ind)] and [(**8a**-H)$_2$Ru(Ind)]$_2$. The products are in equilibrium in solution as indicated by presence of two spectra. Therefore they can be represented by the formulae (Fig. 2.16), while the ^{1}H NMR spectrum of this mixture is presented in Fig. 2.14 c.

Two peaks observed in mass spectrum (Fig. 2.15) correspond to {[(**8a**-H)$^-$]$_2$Ru(Ind) + H$^+$} (calculated for $C_{55}H_{56}N_4O_2Ru+H^+$ 907.3252, observed 907.3498) and to {[(**8a**-H)$^-$]$_2$Ru(Ind)}$_2$ + H$^+$} (calculated for $C_{110}H_{112}N_8O_4Ru_2+H^+$ 1813.697, observed 1813.6917). Both molecular ion peaks reveal proper hyperfine structure related to abundant ruthenium isotopes in comparison with the simulated ones (^{96}Ru, 5.51%;^{98}Ru, 1.87%; ^{99}Ru, 12.72%; ^{100}Ru, 12.62%; ^{101}Ru, 17.07%; ^{102}Ru, 31.61%; ^{104}Ru, 18.58%).

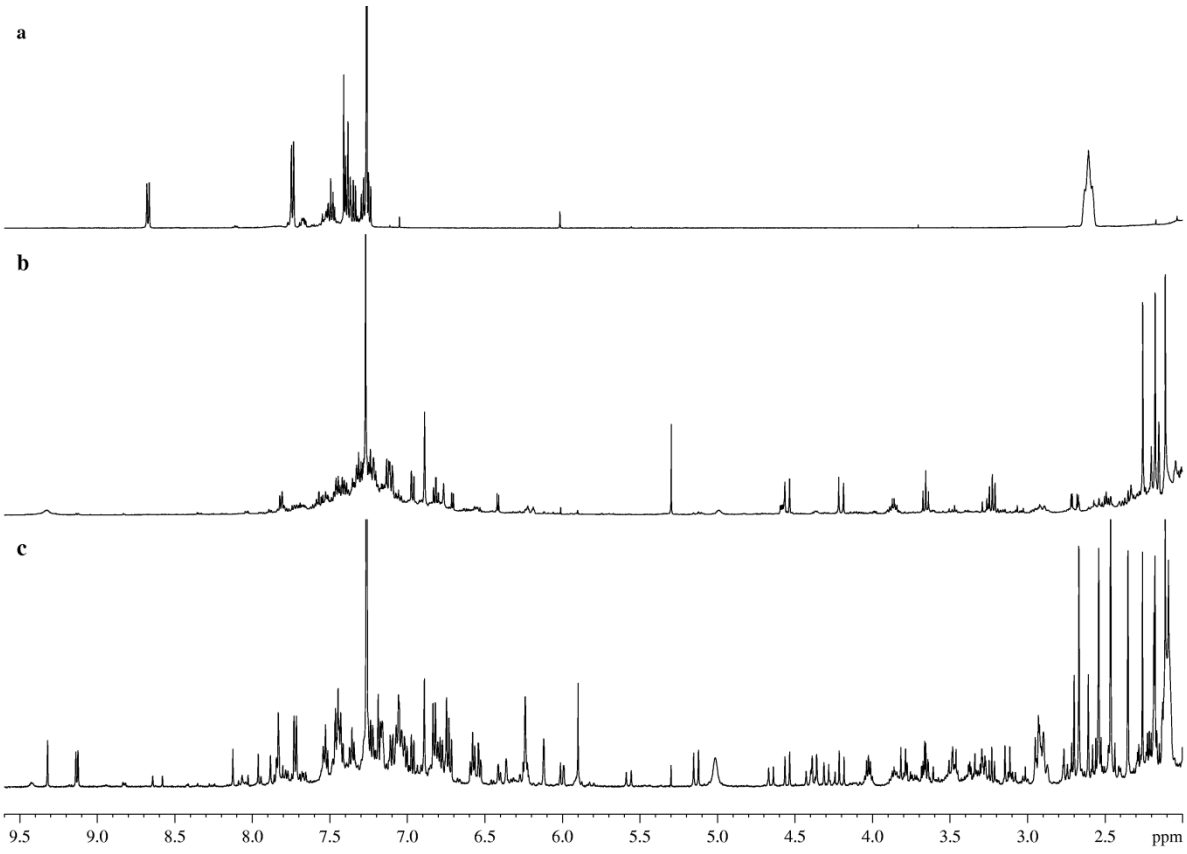


Fig. 2.14 ^{1}H NMR spectra of: a) starting indenylidene Ru complex **16**, b) isolated complex **20** and c) obtained complex **21**, in $CDCl_3$.

In the ^{1}H NMR spectrum the diagnostic proton resonance of the indenylidene ligand is shifted 0.50 ppm downfield from 8.65 in the complex **16** to 9.15 in the complex **21**. Moreover, the downfield resonance from salicylic OH was absent in the spectrum of **21**, indicating the involvement of salicylate oxygen as donor atom. All attempts to crystallize **21** from the dark-red mixture failed till now.

According to the spectral assignments the probable formulae of mono- and di-nuclear ruthenium complexes can be represented as Fig. 2.6.

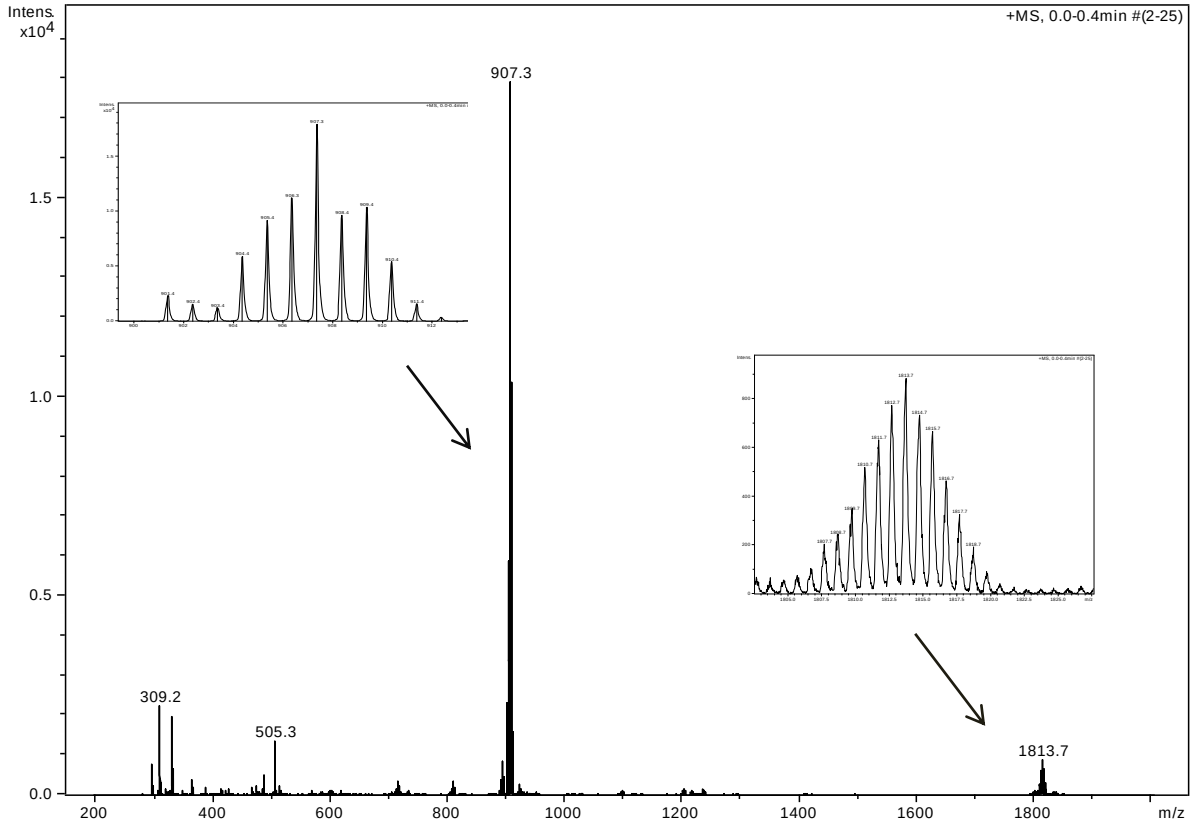


Fig. 2.15 Mass spectrum of ruthenium complexes **21** of the general formula $\{[(8a\text{-}H)^{-}]_2Ru(Ind)\}_n$.

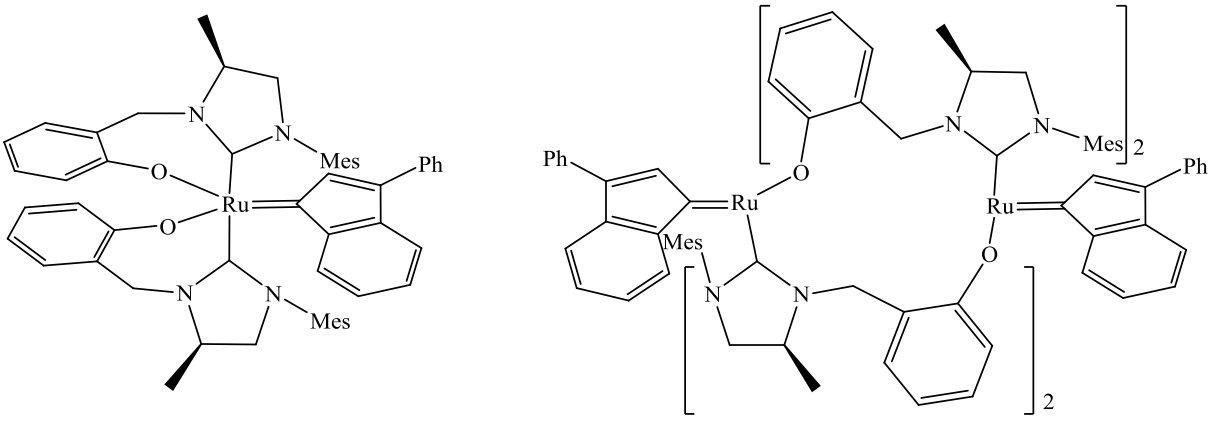
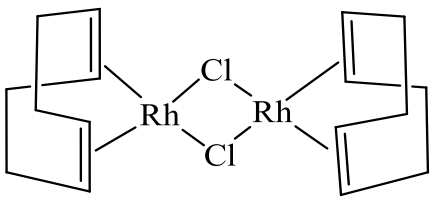


Fig. 2.16 The formulae of the monomeric and one of many possible dimeric compounds of the general composition $\{[(\mathbf{8a}\text{-H})^-]_2Ru(Ind)\}_n$, where n = 1 (monomeric pentacoordinate formula, left side) or n=2 (dimers). There are four possible dimeric compounds with all $(\mathbf{8a}\text{-H})^-$ C,O- or O,C bridging ligands and many dimers with two C,O- or O,C- bridging $(8a\text{-H})^-$ ligands and two C,O chelated ligands into two ruthenium(II) centers.

2.3.2 Coordination of 8a to rhodium(I)

Rhodium(I) is a useful catalytic cation. The Rh(I) complexes containing *N*-heterocyclic carbenes were developed and used as catalysts for hydrosilylation reactions[169]. We have explored the coordination ability of imidazolinium cation **8a** to Rh(I). The convenient starting material to perform this chemistry is dirhodium complex **22** which is stable and soluble in organic solvents.



22

Fig. 2.17 Bis(1,5-cyclooctadiene)dirhodium (I) dichloride complex.

The reaction of **8a** with **22** was performed in toluene or THF with *t*BuOK or K_2CO_3 as a base. In all cases the ^1H NMR spectrum of isolated post-reaction mixture showed formation of two products. Product separation *via* flash column chromatography on silica gel did not lead

to separation and finally the mixture of products in 5:1 molar ratio was obtained as demonstrated by the ^{1}H NMR spectrum (Fig. 2.18).

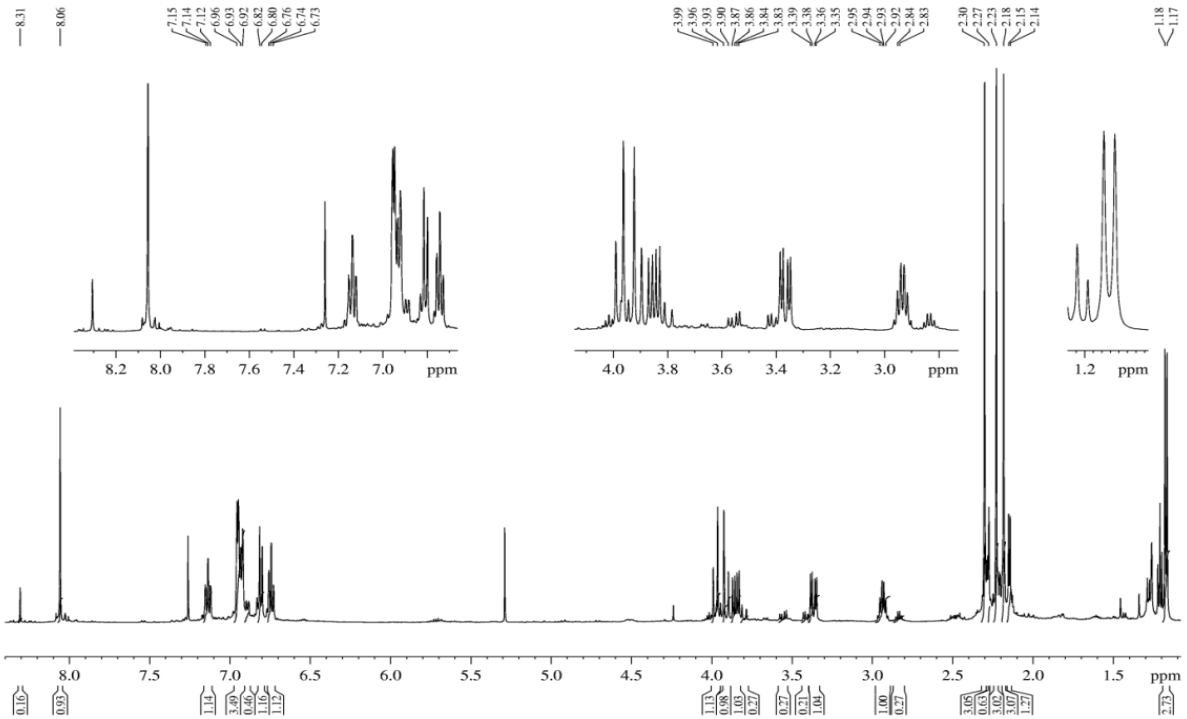


Fig. 2.18 The ^{1}H NMR spectrum of mixture of Rh(I) complexes in $CDCl_3$.

None of two products showed resonances from starting cyclooctadiene ligand. In basic condition applied in synthesis, the cation of **8a** was converted into neutral molecule and coordinated to Rh(I). The downfield resonance from salicylic OH was absent in the spectrum of the products, indicating the involvement of salicylate oxygen as donor atom. Coordination shift was 0.93 ppm for –N-C*H*=N- proton and benzyl methylene protons. The largest coordination shift (1.34 ppm) was found for methine proton. All ligand resonance signals were upfield shifted.

Moreover presence of cross peak between methine proton at 2.94 ppm and adjacent methyl group protons and one of the adjacent methylene protons in COSY experiment was observed for the more abundant form.

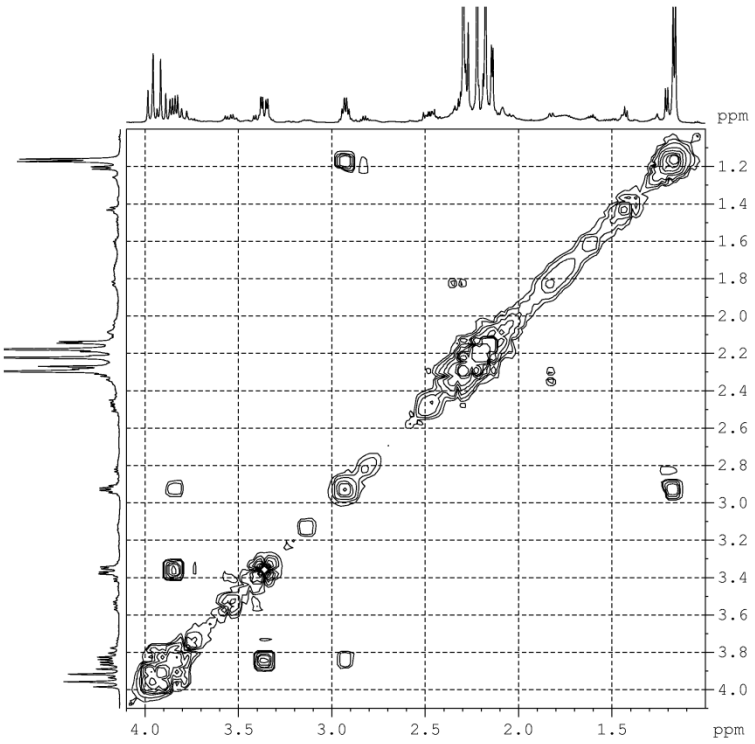


Fig. 2.19 Fragment of COSY spectrum of Rh(I) complex mixture in $CDCl_3$.

This indicates formation of complex with neutral imidazolyl ligand coordinated *via* O and C atoms rather that coordination of carbene itself. The chloride anions remained coordinated. Considering the geometry of two rhodium(I) centers the formation of two isomers: extended *cis* and extended *trans* (Fig. 2.20) are expected. These two isomers convert slowly at NMR time-scale, they cannot be separated, however, chromatographically. The attempts to crystallize this material failed.

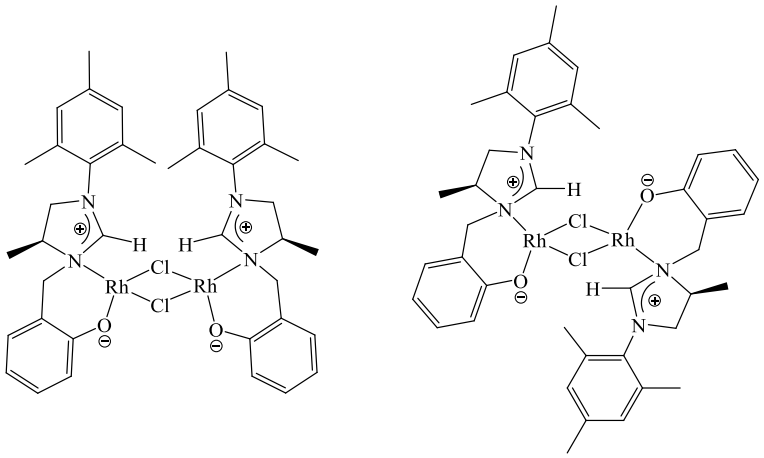
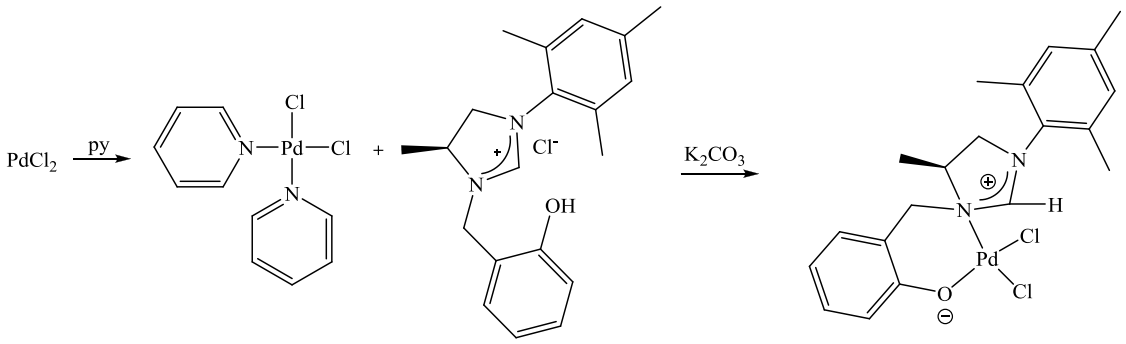


Fig. 2.20 Extended *cis* and extended *trans* isomers of Rh complexes, (**23**).

2.3.3 Coordination of 8a to palladium(II)

Similarly to ruthenium(II) and rhodium(I), also the palladium(II) is inert enough to follow the ligation reaction and diamagnetic, which enables to characterize the reaction products with ^{1}H NMR spectroscopy. Therefore I have tested coordination ability of **8a** to palladium. The simple palladium dichloride salt is poorly soluble in any solvent, therefore the $Pd(py)_2Cl_2$ was generated in situ in pyridine or pyridine-d_5 for NMR spectral monitoring of the reaction progress. Additionally K_2CO_3 was used as base in order to ensure deprotonation of cationic **8a**.



8a

Scheme 2.8 Scheme of synthesis of NHC Pd-complex, (**24**).

After 24 hours of stirring a ^{1}H NMR spectrum of the post reaction mixture in pyridine-d_5 was recorded (Fig. 2.21).

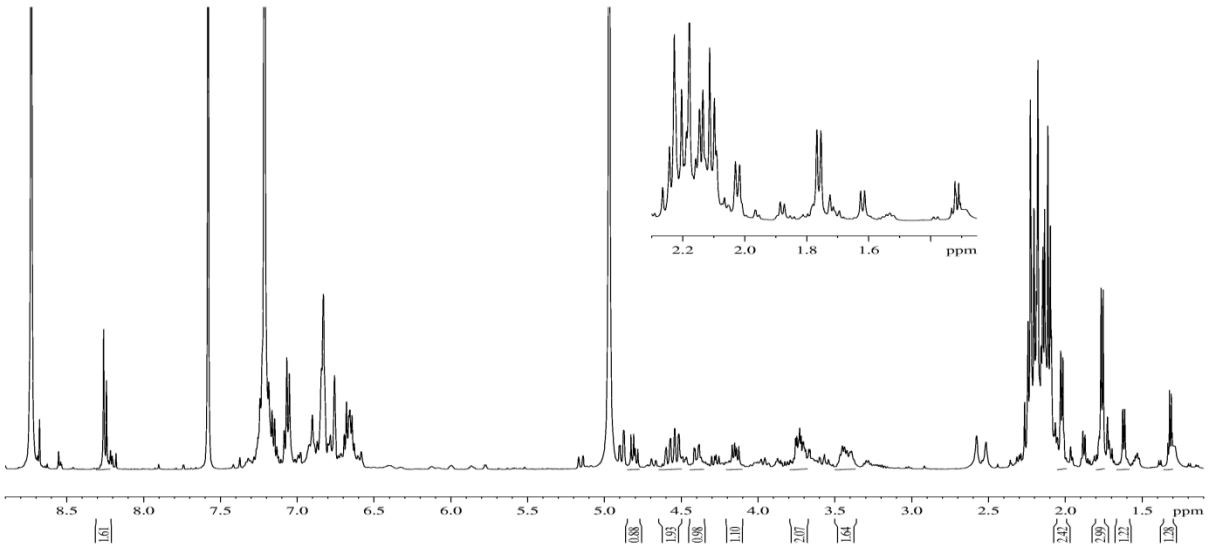


Fig. 2.21 ^{1}H NMR spectrum of post reaction mixture in pyridine-d_5.

Five doublets with different intensity in the region 2.1-1.4 ppm that are diagnostic resonances for methyl group protons at stereogenic center as well as a group of singlets between 2.3-2.1 ppm that are characteristic resonances for methyl groups protons of the mesityl substituents indicated the presence of at least five products.

Likewise in previous cases we were able to isolate a fraction of isomers using flash column chromatography on silica gel. Also in case of square planar complexes of palladium(II) we obtained the mixture of two compounds. The ^{1}H NMR spectrum of this mixture is shown in Fig. 2.22. Presence of two doublets at 1.46 ppm and 3.38 ppm diagnostic for the methyl group attached to chiral carbon and coupled with its methine proton.

Since pyridine-d_5 was used no resonances of pyridine ligand was observed in $CDCl_3$. Therefore the synthesis was performed according to the same protocol with pyridine. The mixture of products was obtained.

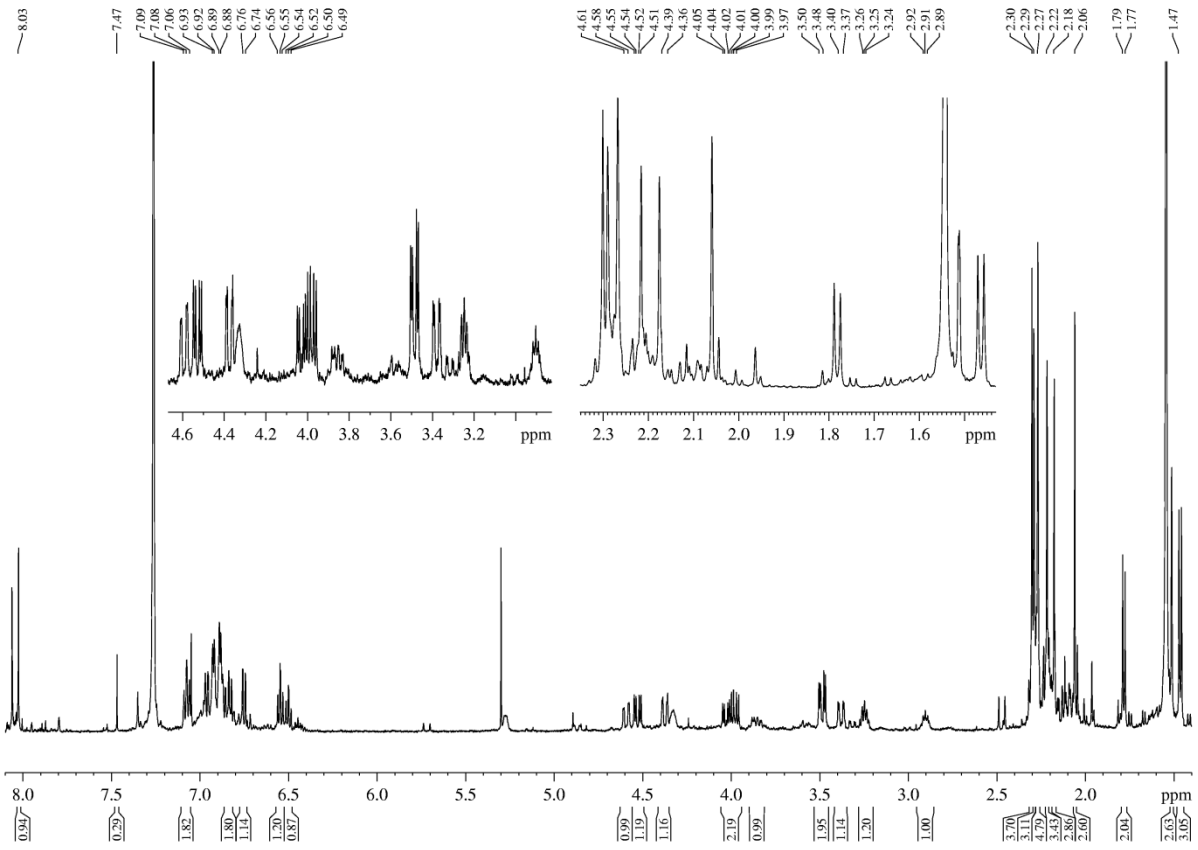


Fig. 2.22 The ^{1}H NMR spectrum of mixture of palladium(II) isomers in $CDCl_3$.

Cross peaks between two separate methine protons at 2.94 and 3.34 ppm and adjacent methyl group protons at 1.75, and 1.45 ppm, respectively were observed in COSY experiment while no cross peaks of the adjacent methylene protons were observed (Fig. 2.23).

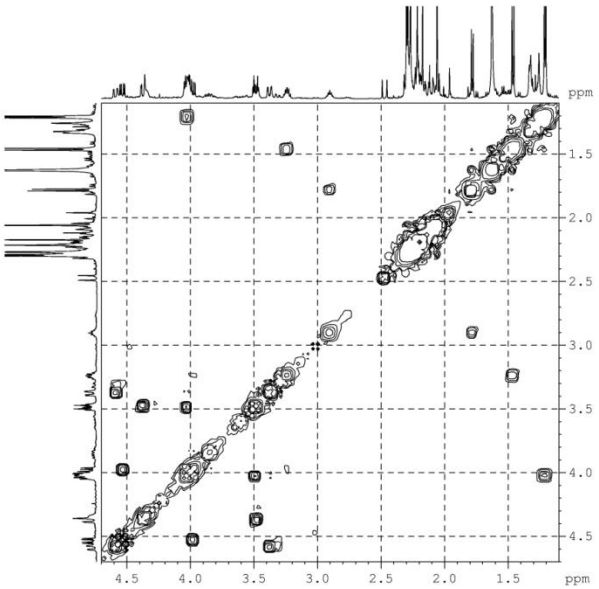


Fig. 2.23 Fragment of COSY spectrum of Pd(II) complex mixture in $CDCl_3$.

2.4 Modified PAMAM dendrimers

Dendrimer is a particular case of polymer with multiple branches and it is made by successive growth of polyfunctional monomers onto an initiator with multiple functionality. This gives rise to a tree-like structure with the number of branches increasing away from a center. The spectrum of dendrimer families is now very broad and have been accurately described and reviewed[170]. The properties of dendrimers were first examined with Tomalia's polyamidoamine (PAMAM) dendrimers that are now commercial.[171] Since our group was investigating this class of dendrimers we decided to use this structures for immobilization of Ru-complexes on their surfaces[172] and studied their potential catalytic activity as heterogeneous catalyst for olefin metathesis reactions.

2.4.1 Synthesis of PAMAM dendrimers

Following Tomalia's procedure[173] I prepared the 3rd generation of PAMAM dendrimer. It was synthesized by the divergent method with ethylenediamine as a core. This method involved a two-step iterative sequence to produce either ester or amine terminated structures. Sequence is composed of (a) alkylation with methyl acrylate followed by (b) amidation with excess of ethylenediamine. We obtained amine terminated dendrimer with thirty two $-NH_2$ groups. Shorthand designation of this structure is **G3-PAMAM(-NH_2)$_{32}$**. Its structure is shown in Fig. 2.24.

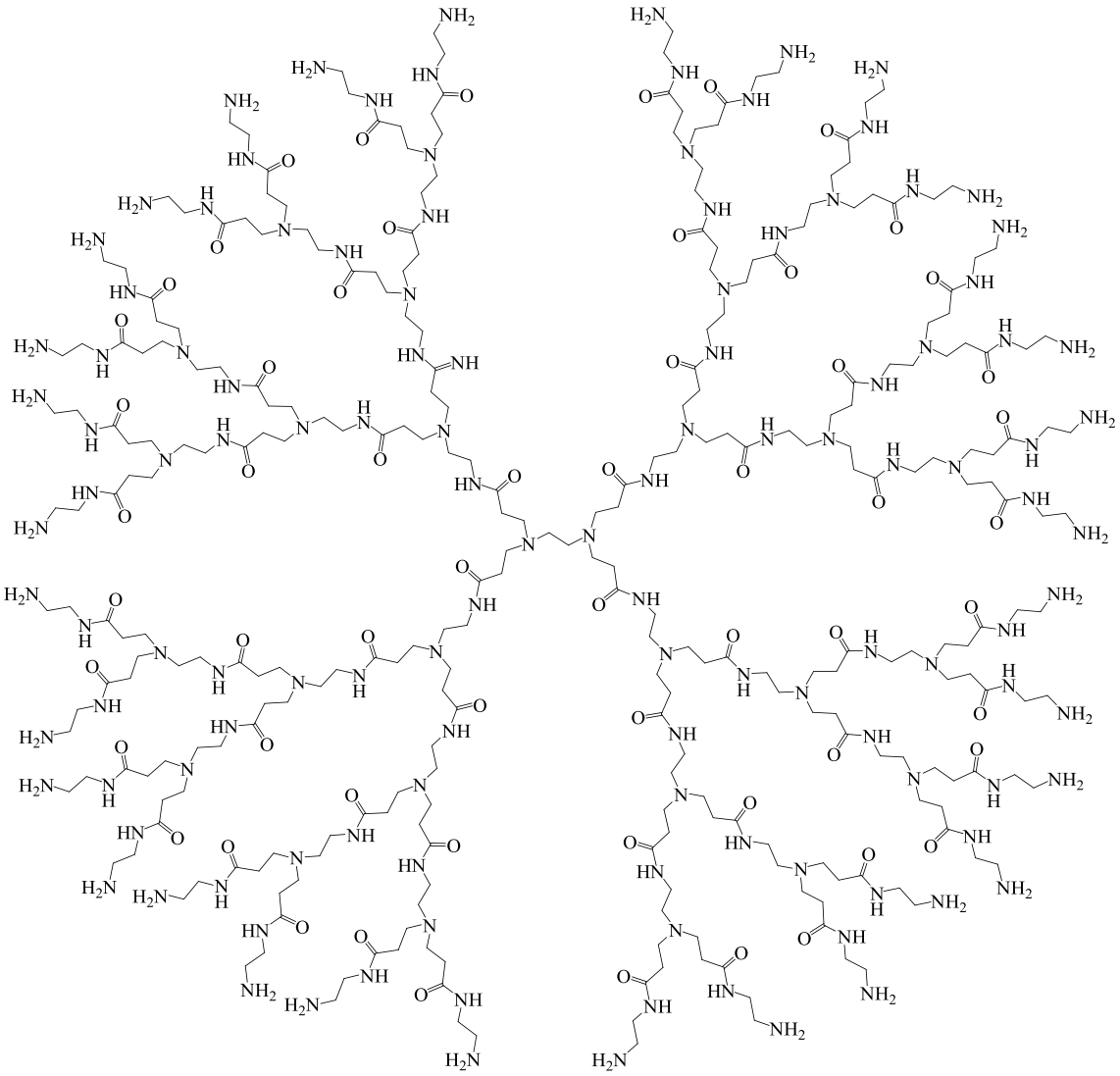
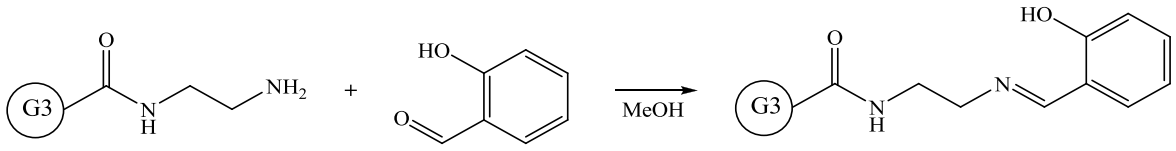


Fig. 2.24 Structure of the 3rd generation PAMAM dendrimer **G3-PAMAM(-NH_2)$_{32}$**.

Then I modified the terminating group *via* condensation of **G3-PAMAM(-NH_2)$_{32}$** with salicyl aldehyde to form Schiff bases on the periphery of the dendrimer. I have obtained the conjugate G3-PAMAM(-NH_2)$_{32}$ with 50% and 100% amine groups substituted with salicylic residue attached *via* aldimine bonds (Scheme 2.9).

The reaction was performed in MeOH using 16 and 32 salicyl aldehyde equivalents to obtain half- and thoroughly condensed terminal groups respectively. I determined the degree of conversion using ^{1}H NMR spectroscopy. To estimate the degree of aldehyde substitution we compared the integration of characteristic resonance signals at 2.15 ppm (corresponding to [64H]) ppm from the dendrimer and resonance signals of the -N=CH- protons at 8.45 ppm. In the Fig. 2.25 the ^{1}H NMR spectra of obtained products are compared.



Scheme 2.9 Scheme of reaction between **G3-PAMAM(-NH_2)$_{32}$** and salicylic aldehyde.

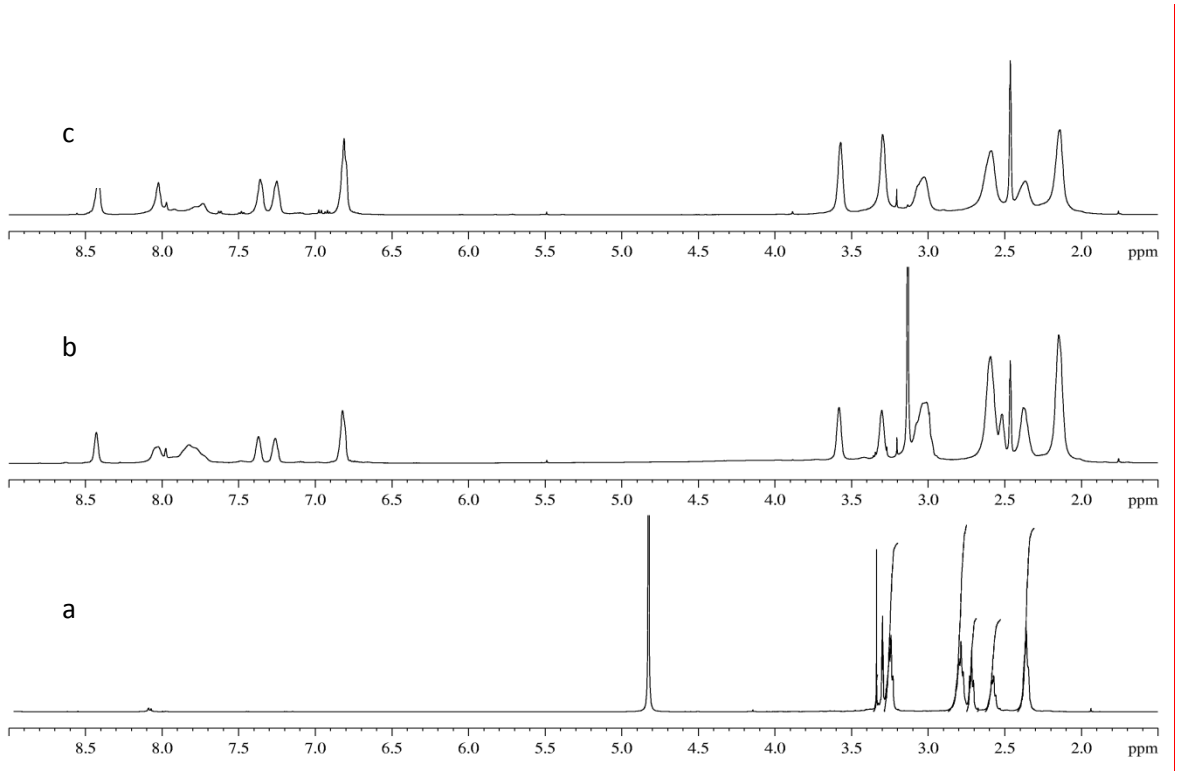


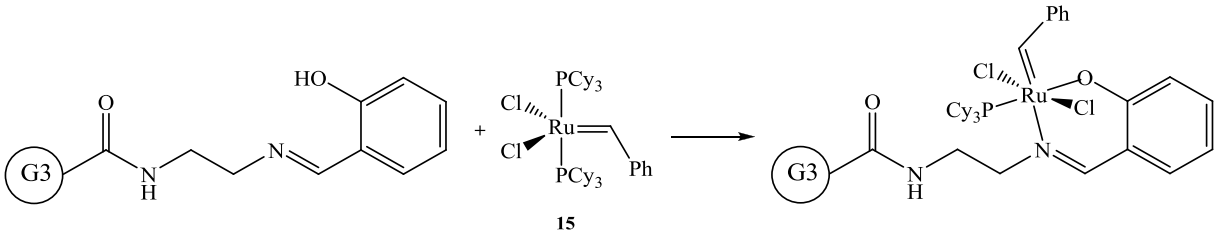
Fig. 2.25 The ^{1}H NMR spectra of a) **G3-PAMAM(-NH_2)$_{32}$** in CD_3OD, b) **G3-PAMAM(-NH_2)$_{32}^{50Sal}$** in DMSO-d_6, c) and **G3-PAMAM(-NH_2)$_{32}^{100Sal}$** in DMSO-d_6.

2.4.2 Immobilization of Ru-complexes

Schiff base ruthenium complexes and their applications in catalytic processes were described by Verpoort group. This group of complexes were tested towards ring closing metathesis reaction or for the COD polymerization.[174]

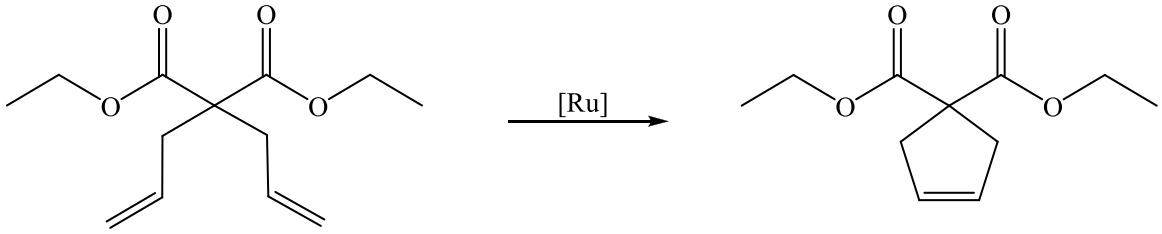
We use prepared **G3-PAMAM^{50Sal}** as a polymer support for Ru-complex **15**.

After reaction of **G3-PAMAM^{50Sal}** with Ru-complex **15** were separated as heterogeneous catalyst in form of a violet powder.



Scheme 2.10 Immobilization reaction of Ru-complex **15** on **G3-PAMAM^{50Sal}**.

Catalytic activity of this compound was checked towards ring closing metathesis reaction of diethyl diallyl malonate (Scheme 2.11) using standard ^{1}H NMR procedure.[175]



Scheme 2.11 Standard example of RCM of diethyl diallyl malonate.

I observed only maximum 65% conversion.

Since the color of obtained violet product quickly convert into green that was completely inactive in test reaction as well as because of low conversion we have concluded that obtained heterogeneous catalyst was not promising.

2.5 Conclusions

Synthesis of imidazolinium salts bearing ring-centered chirality was performed starting from *N*-Boc derivatives of L-alanine and L-phenylalanine as examples of amino acid pool representatives. The following steps of synthetic route comprised: 1) conversion of carboxylate into *N*-aryl amide *via* DCC activation of carboxylic group, 2) removal of Boc group from amine group, 3) condensation of released amine group with aromatic aldehyde, 4) total or partial (stepwise) reduction of amide carbonyl and aldimine groups, 4) closure of imidazolyl ring with triethylformate. The compounds were characterized by NMR and IR spectroscopy and MS spectrometry, as well as other appropriate methods, like polarimetry.
The following cationic imidazolyl ligands were isolated as chloride salts: (*S*)-1-(2-hydroxybenzyl)-3-mesityl-5-methyl-4,5-dihydro-1*H*-imidazol-3-ium chloride **8a**; (*S*)-1-(3,5-di-*tert*-butyl-2-hydroxybenzyl)-3-mesityl-5-methyl-4,5-dihydro-1*H*-imidazol-3-ium chloride **8b**; (*R*)-1-(2-hydroxybenzyl)-3-mesityl-5-methyl-4,5-dihydro-1*H*-imidazol-3-ium chloride **8c**; (*R*)-1-(3,5-di-*tert*-butyl-2-hydroxybenzyl)-3-mesityl-5-methyl-4,5-dihydro-1*H*-imidazol-3-ium chloride **8d**; (*S*)-4-benzyl-3-(2-hydroxybenzyl)-1-mesityl-4,5-dihydro-1*H*-imidazol-3-ium chloride **13**.

Cationic imidazolylidene ligand **8a** was used further to obtain the transition metal complexes with ruthenium(II), rhodium(I) and palladium(II) ions. When $Cl_2(PCy_3)_2$Ru-(indenylidene) starting ruthenium(II) complex, (**16**), was reacted with ligand **8a** in toluene and KHMDS, the isolated product had the formula $[(\mathbf{8a}\text{-H})_2\text{Ru(indylidene)}]_n$ (n = 1 or 2), identified by mass and NMR spectra. The anionic ligand **8a** was coordinated *via* phenolic oxygen and imidazolylidene carbon. The pentacoordinate complex was in equilibrium between monomeric species (n = 1) and dimer (n = 2), in which the **8a** was a bridging ligand. In case of rhodium(I) and palladium(II) all attempts to obtain complexes with O,C-chelated imidazolylidene anion failed; instead the neutral ligand was very likely coordinated *via* phenolic oxygen, although clearly involving the phenolate oxygen but not HNC or even aminidinium species could not be established despite many attempts.

The attempts to immobilize ruthenium(II) catalyst for ring closing metathesis led to heterogeneous catalytic material of moderate activity. The PAMAM-immobilized ruthenium(II) compound was unstable in catalytic reaction conditions and bleached after one catalytic cycle.

Part 3

3. Experimental

3.1 Materials

Starting reagents amino acids with the amino group protected by *t*-butoxycarbonyl (boc) were purchased from Sigma-Aldrich and were used as received. Bis(tricyclohexylphosphine)-3-phenyl-1*H*-inden-1-ylideneruthenium(II) dichloride, **16** was purchased from Strem Chemicals, Inc. and used as received. All other chemical compounds were purchased from Sigma-Aldrich and used without further purification. All solvents were dried with appropriate drying agents and distilled prior to use.

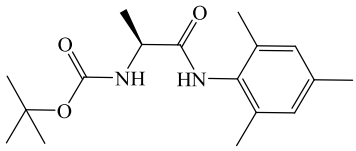
All reactions and manipulations involving organometallic compounds were conducted in oven-dried glassware under argon atmosphere unless otherwise noted. Flash chromatography was performed using silica gel 60. Reactions progress was monitored by TLC chromatography using TLC silica gel 60 F_{254} plates.

3.2 Measurements and equipment

^{1}H, ^{13}C and ^{31}P NMR measurements were performed with a Bruker Avance II 500 spectrometer and are reported in parts per million (ppm) with TMS as reference or using the residual solvent peak. Coupling constant *J* is given in Hz.
Infra-red (IR) spectra were obtained using NICOLET 8700 FT-IR, Thermo SCIENTIFIC spectrometer with the % transmittance values reported in cm^{-1}. Melting points were measured using MEL-TEMP® Electrothermal apparatus. Optical rotations $[\alpha]_D^{20}$ were performed on a Jasco P-1020 polarimeter apparatus operating at 20 ºC. Elemental analysis was carried out on AE 1108 Carlo Erba analyzer. Mass spectra were recorded on Bruker AuflexSpeed spectrometer.

3.3 Syntheses

3.3.1 Synthesis of imidazolylidene ligands



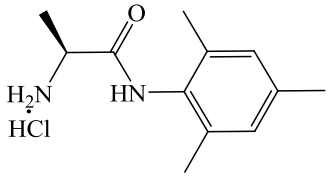
(*S*)-*tert*-butyl 1-(mesitylamino)-1-oxopropan-2-ylcarbamate, 1

2,4,6-Trimethylaniline (2.1 mL, 15 mmol) was added to a solution of Boc-L-alanine (2.8 g, 15 mmol) in dry THF (50 mL) followed by addition of DCC (3.1 g, 15 mmol) solution in dry THF (30 mL). The mixture was stirred at room temperature for 18 h. Subsequently white precipitate was filtered off and filtrate was concentrated by rotary evaporator. The oily filtrate residue was purified by silica gel chromatography (DCM/MeOH) to give compound **1** (4.3 g, 93%) as colorless solid. M. p.: 118-120 ºC.

^{1}H-NMR ($CDCl_3$): δ 7.55 (bs, 1H, N*H*), 6.85 (s, 2H, Ar*H*), 5.14 (bs, 1H, N*H*), 4.33 (m, 1H), 2.24 (s, 3H, ArCH_3), 2.13 (s, 6H, ArCH_3) 1.46 (d, *J*=9.8, 3H), 1.44 (s, 9H).

^{13}C-NMR ($CDCl_3$): δ 171.5 (*C*O), 156.0 (*C*ONH), 137.1, 135.3 (2x*C*), 130.9, 129.1 (2xC_{ArH}), 80.4, 50.5, 28.5, 21.1, 18.4 (3x*C*).

IR (KBr): 3303.9, 2979.9, 2930.8, 2853.1, 1712.9, 1683.5, 1658.9, 1529.7, 1459.3, 1402.0, 1367.3, 1319.8, 1295.5, 1270.4, 1253.5, 1225.1, 1161.4, 1067.9, 1005.7.



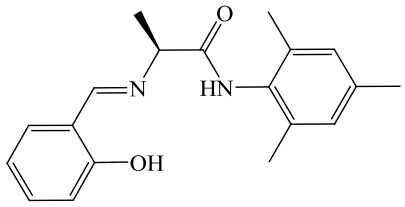
(*S*)-2-amino-*N*-mesitylpropanamide hydrochloride, 2

A compound **1** (2.3 g, 7.5 mmol) and HCl solution in diethyl ether (2M, 25 mL) were stirred at room temperature for 5 h. Afterwards white precipitate was filtered off and washed with diethyl ether to give compound **2** (1.5 g, 82%) as colorless solid. M. p.: 257-259 ºC.

^{1}H-NMR (DMSO-d_6): δ 9.88 (s, 1H, N*H*), 8.32 (bs, 3H, NH_2), 6.89 (s, 2H, ArH), 4.10 (q, *J*=6.9, 1H), 2.22 (s, 3H), 2.11 (s, 6H), 1.52 (d, *J*=6.9, 3H).

^{13}C-NMR (DMSO-d_6): δ 168.1 (*C*O), 135.8, 134.8, 131.3, 128.3 (2xC_{ArH}), 48.3 (*C*HCO), 20.5, 17.9 (2x*C*), 17.5.

IR (KBr): 3274.1, 2916.8, 2857.5, 2664.2, 2588.5, 2456.4, 1671.5, 1611.2, 1587.1, 1540.8, 1469.0, 1391.9, 1377.4, 1245.3, 1199.5, 1126.7, 1100.2, 997.5, 977.8, 957.0, 845.6.



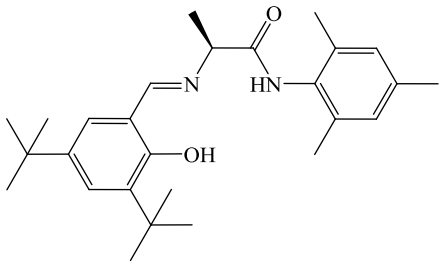
(*S*)-2-(2-hydroxybenzylideneamino)-*N*-mesitylpropanamide, 3a

MeONa was added to a solution of **2** (1.5 g, 6.2 mmol) in MeOH (35 mL) until reaction mixture gained neutral pH. Afterwards salicylaldehyde (0.65 mL, 6.2 mmol) was added and resulting mixture was stirred at room temperature for 16 h. A yellow solid was filtered off and washed with water and hexane to give compound **3a** (1.6 g, 83%). M.p.: 166-167 ºC. $[\alpha]_D^{20}$= +171 (c 1, $CHCl_3$).

^{1}H-NMR ($CDCl_3$): δ 12.45 (s, 1H, O*H*), 8.50 (s, 1H, C*H*=N), 7.38 (t, *J*=7.4, 1H), 7.36-7.33 (m, 2H), 7.31 (bs, 1H), 7.00 (d, *J*=8.3, 1H), 6.95 (t, *J*=7.4, 1H), 6.87 (s, 2H, Ar*H*), 4.20 (q, *J*=6.9, 1H), 2.25 (s, 3H), 2.15 (s, 6H), 1.68 (d, *J*=6.9, 3H).

^{13}C-NMR ($CDCl_3$): δ 170.6 (*C*O), 166.9 (*C*=N), 160.6, 137.2, 134.9, 133.3, 132.2, 130.5, 129.0 (2xC_{ArHMes}), 119.4, 118.5, 117.1, 69.2, 21.3, 20.9, 18.2 (2x*C*).

IR (KBr): 3254.3, 2915.8, 1659.9, 1635.3, 1525.4, 1462.3, 1387.1, 1296.4, 1278.6, 1232.8, 1224.6, 1101.6, 1048.6, 987.4, 903.0, 851.4, 750.7, 716.4, 460.4.



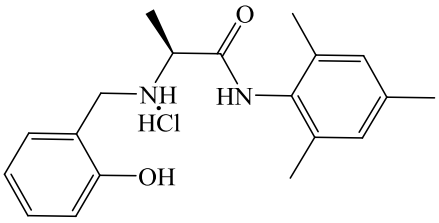
(*S*)-2-(3,5-di-*tert*-butyl-2-hydroxybenzylideneamino)-*N*-mesitylpropanamide, 3b

MeONa was added to a solution of compound **2** (1.3 g, 5.4 mmol) in MeOH (30 mL) untill reaction mixture gained neutral pH. Afterwards, 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (1.2 g, 5.1 mmol) was added and resulting mixture was stirred at room temperature for 16 h. A yellow solid was filtered off and washed with water and hexane to give compound **3b** (1.8 g, 83%). M. p.: 234-236 ºC.

^{1}H-NMR ($CDCl_3$): δ 12.88 (s, 1H, O*H*), 8.51 (s, 1H, C*H*=N), 7.46 (d, *J*=2.4, 1H), 7.41 (bs, 1H, N*H*CO), 7.17 (d, *J*=2.4, 1H), 6.89 (s, 2H, Ar*H*), 4.18 (q, *J*=6.9, 1H), 2.26 (s, 3H), 2.18 (s, 6H), 1.69 (d, *J*=6.9, 3H), 1.44 (s, 9H), 1.32 (s, 9H).

^{13}C-NMR ($CDCl_3$): δ 170.8 (*C*O), 168.0 (*C*=N), 157.7 (C_{Ar}OH), 141.0, 137,1, 137.0, 135.0 (2x*C*), 130.6, 129.0 (2xC_{ArHMes}), 128.2, 126.7, 117.6, 69.4, 35.1, 34.2, 31,5, 29.4, 21.5, 20.9, 18.3 (2x*C*).

IR (KBr): 3219.1, 3052.3, 2953.9, 2915.8, 2869.1, 1655.6, 1608.8, 1545.2, 1466.1, 1440.6, 1361.0, 1276.2, 1248.2, 121.5, 1136.8, 1057.8, 882.3, 850.9, 774.3, 695.2.



(*S*)-2-(2-hydroxybenzylamino)-*N*-mesitylpropanamide hydrochloride, 4a

$NaBH_4$ (0.16 g, 4.2 mmol) was added to a solution of compound **3a** (0.50 g 1.6 mmol) in dry THF (30 mL). The mixture was stirred at room temperature for 16 h and then at reflux temperature for 2 h. Thereafter, the reaction mixture was cooled down and distilled water was added. After *ca* 4 h white precipitate was filtered off and dried to give (*S*)-2-(2-hydroxybenzylamino)-*N*-mesityl-propanamide (0.37 g, 74%) as colorless solid.

^{1}H-NMR ($CDCl_3$): δ 7.28 (bs, 1H, OH), 7.20 (t, *J*=7.7, 1H, Ar*H*), 7.03 (d, J=7.7, 1H, Ar*H*), 6.92 (s, 2H, Ar*H*), 6.88-6.79 (m, 2H, Ar*H*), 4.20 (d, *J*=13.6, 1H), 3.83 (d, *J*=13.4, 1H), 3.41 (q, *J*=7.5, 1H), 2.28 (s, 3H), 2.18 (s, 6H), 1.55 (d, *J*=7.3, 3H).

^{13}C-NMR ($CDCl_3$): δ 172.5 (CO), 157.9 (C_{Ar}OH), 137.4, 134.9, 130.5, 129.1, 128.8, 122.0, 119.4, 116.5, 55.9, 50.6, 20.9, 20.0, 18.4.

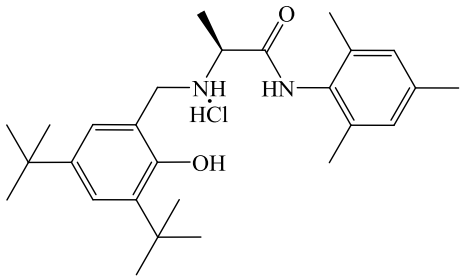
A solution of HCl in diethyl ether (1M, 0.5 mL) was added to a solution of (*S*)-2-(2-hydroxybenzylamino)-*N*-mesitylpropanamide (0.33 g, 1.1 mmol) in chloroform (9 mL). The mixture was stirred at room temperature for 3 h. Afterwards, a white precipitate was filtered off and washed with diethyl ether to give compound **4a** (0.33 g, 90%) as a colorless solid.

^{1}H-NMR (DMSO-d_6): δ 10.27 (bs, 1H), 10.14 (s, 1H), 9.46 (bs, 1H), 9.15 (bs, 1H), 7.44 (d, *J*=6.3, 1H), 7.23 (t, *J*=6.6, 1H), 7.00 (d, *J*=7.8, 1H), 6.90 (s, 2H), 6.84 (t, *J*=7.4, 1H), 4.18 (bs, 1H), 4.10 (bs, 2H), 2.23 (s, 3H), 2.13 (s, 3H), 1.62 (d, *J*=6.9, 3H).

^{13}C-NMR (DMSO-d_6): δ 167.2 (*C*O), 156.0 (C_{Ar}OH), 135.9, 134.7, 131.5, 131.2 (2x*C*), 130.3, 128.4 (2x*C*), 118.9, 117.9, 115.5, 55.1, 43.7, 20.5, 18.0 (2x*C*), 16.5.

IR (KBr): 3042.3, 1660.0, 1608.3, 1525.8, 1505.6, 1486.0, 1462.3, 1378.7, 1354.1, 1317.7, 1270.0, 855.7, 759.3.

MS(ESI): m/z calculated for $C_{19}H_{25}N_2O_2$ $[M+H]^+$ 313.1838, observed 313.1802.



(*S*)-2-(3,5-di-*tert*-butyl-2-hydroxybenzylamino)-*N*-mesitylpropanamide hydrochloride, 4b

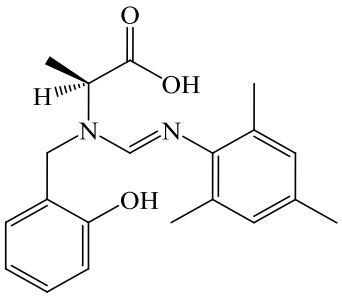
$NaBH_4$ (0.15 g, 4.0 mmol) was added to a solution of compound **3b** (0.50 g 1.2 mmol) in dry THF (30 mL). The mixture was stirred at room temperature for 16 h and then at reflux temperature for 2 h. Thereafter, the reaction mixture was cooled down and distilled water was added. After *ca* 4 hours a white

precipitate was filtered off and dried to give (*S*)-2-(3,5-di-*tert*-butyl-2-hydroxybenzylamino)-*N*-mesitylpropanamide as colorless solid.

Conc. HCl*aq* (0.2 mL) was added to a solution of (*S*)-2-(3,5-di-*tert*-butyl-2-hydroxy-benzylamino)-*N*-mesitylpropanamide in chloroform (9 mL). The mixture was stirred at room temperature for 3 h. Afterwards, a white precipitate was filtered off and washed with diethyl ether to give compound **4b** (0.35 g, 65%) as a colorless solid.

^{1}H-NMR (CD_3OD): δ 7.40 (d, *J*=2.4, 1H), 7.27 (d, *J*=2.4, 1H), 6.92 (s, 2H), 4.31-4.21 (m, 3H), 2.25 (s, 3H), 2.18 (s, 6H), 1.73 (d, *J*=7.4, 3H), 1.40 (s, 9H), 1.29 (s, 9H).

^{13}C-NMR (CD_3OD): δ 168.0, 151.7 ($C_{Ar}OH$), 143.8, 139.4, 137.4, 134.9 (2x*C*), 130.2, 128.5 (2x*C*), 125.7, 125.5, 120.4, 55.7, 46.5, 34.6, 33.9, 30.5, 29.1, 19.6, 17.1 (2x*C*), 15.9.



(*S,E*)-2-(*N*-(2-hydroxybenzyl)-*N'*-mesitylformamimidamido) propanoic acid, 6

A compound **4a**·(0.30 g, 1.4 mmol) was suspended in dry toluene (15 mL). Afterwards $(EtO)_3CH$ (2.5 mL) was added. The reaction mixture was stirred at reflux temperature for 6 hours. Afterwards the mixture was cooled down and stirred at room temperature for 12 h. Then solvent was removed in vacuo. A dry residue was purified by silica gel chromatography (DCM/*i*PrOH). The mixture of products **6** and **6'**, in 1.0:0.8 molar ratio were isolated (~35%).

^{1}H NMR (DMSO-d_6): two set of resonances of relative intensity 1:0.7:

δ 9.57 (s, 1H), 9.37 (s, 1H), 8.46 (s, 1H), 7.09-7.03 (m, 2H), 6.87 (s, 2H), 6.83-6.78 (m, 1H), 6.75 (t, *J*=7.5, 1H), 4.62-4.49 (m, 1H), 4.37 (q, *J*=7.5, 1H), 4.29 (d, *J*=16.0, 1H), 2.21 (s, 3H), 2.05 (s, 6H), 1.49 (d, *J*=7.5, 3H).

δ 9.78 (s, 1H), 8.93 (s, 1H), 8.28 (s, 1H), 7.20 (d, *J*=7.5, 1H), 7.12 (td, *J*=7.5, 1.5, 1H), 6.85 (s, 2H), 6.83-6.78 (m, 2H), 4.62-4.49 (m, 3H), 2.21 (s, 3H), 2.03 (s, 6H), 1.25 (d, *J*=7.5, 3H).

^{13}C NMR (DMSO-d_6): δ 169.6, 169.2, 164.1, 163.3, 155.1, 154.7, 135.5, 135.3, 135.0, 134.7 (2*C*), 132.0, 131.77, 129.3, 128.6, 128.2 (2*C*), 128.1 (3*C*), 127.9, 127.8, 124.0, 123.2, 119.0, 118.8, 115.1, 114.9, 56.0, 52.0, 45.3, 41.2, 20.4 (2C), 17.8 (2*C*), 17.7 (2*C*), 17,4, 14.7.

IR (KBr) : 3250.2, 2920.3, 1655.3, 1608.2, 1510.0, 1487.6, 1458.0, 1398.2, 1375.3, 1352.6, 1295.4, 1240.7, 1105.4, 850.8, 755.6, 730.8.

MS(ESI): m/z calculated for $C_{20}H_{24}N_2O_3$ $[M+Na]^+$ 363.1685, observed 363.1625.

Reaction of (*S*)-2-(3,5-di-*tert*-butyl-2-hydroxybenzylamino)-*N*-mesitylpropanamide hydrochloride, 4b, with triethyl orthoformate.

A compound **4b** (0.30 g, 1.1 mmol) was suspended in dry toluene (15 mL). Afterwards $(EtO)_3CH$ (2.0 mL) was added. The reaction mixture was stirred at reflux temperature for 16 h. Afterwards, the mixture was cooled down and solvent was removed in vacuo. A dry residue was purified by silica gel chromatography (DCM/MeOH).

Two products **5b** and **5b'** were isolated and characterized by NMR spectroscopy:

Product **5b**

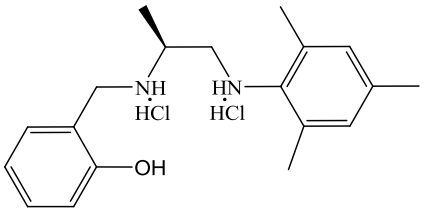
^{1}H-NMR ($CDCl_3$): δ 7.12 (d, *J*=2.0, 1H), 6.96 (bs, 1H), 6.95 (d, *J*=2.0, 1H), 6.87 (bs, 1H), 5.80 (s, 1H), 4.61 (s, 1H), 4.47 (d, *J*=17.0, 1H), 4.31 (d, *J*=17.0, 1H), 3.99-3.92 (m, 1H), 3.89-3.82 (m, 1H), 3.75-3.69 (m, 1H), 3.59-3.52 (m, 1H), 2.39 (s, 3H), 2.29 (s, 3H), 2.23 (s, 3H), 1.56 (s, 3H), 1.32 (t, *J*=7.0, 3H), 1.28 (s, 9H), 1.19 (t, *J*=7.0, 3H), 1.11 (s, 9H).

^{13}C-NMR ($CDCl_3$): δ 173.4 (*C*O), 149.6, 144.1, 138.5, 138.2, 137.8, 135.3, 129.2, 129.1, 123.4, 121.7, 121.4, 107.1, 96.7, 67.6, 67.2, 65.8, 44.7, 34.4 (2x*C*), 31.6, 29.7, 29.5, 21.1, 18.8, 18.4, 17.8, 15.6, 15.4.

Product **5b'**

^{1}H-NMR ($CDCl_3$): δ 8.37 (bs, 1H), 8.17 (bs, 1H), 7.29 (bs, 1H), 6.89 (s, 2H), 5.49 (s, 1H), 4.00-3.92 (m, 1H), 3.86-3.73 (m, 2H), 3.67-3.60 (m, 1H), 2.26 (s. 3H), 2.10 (s, 6H), 1.83 (s, 3H), 1.29 (t, *J*=7.0, 3H), 1.17 (t, *J*=7.0, 3H).

^{13}C-NMR ($CDCl_3$): δ 170.1 (*C*O), 160.5, 136.8, 135.1 (2x*C*), 131.0, 128.8 (2x*C*), 103.2, 66.9, 66.6, 63.5, 21.2, 20.9, 18.2 (2x*C*), 15.5, 15.4.



(*S*)-2-{[1-(mesitylamino)propan-2-ylamino]methyl}phenol dihydrochloride, 7a

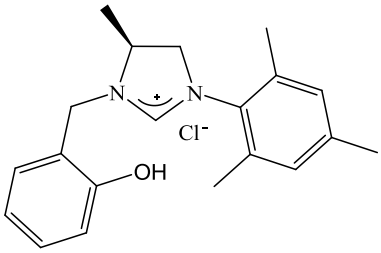
The mixture of compound **3a** (2.0 g, 6.6 mmol) and a solution of BH_3·THF complex (1M, 40 mL) was stirred at reflux temperature for 24 h. Then the mixture was cooled down to room temperature and MeOH was added drop-wise till all bubbling ceased. Conc. HCl*aq* (12M, 1mL) was added and the solvent was removed by evaporation. The resulting solid was redissolved in MeOH and the solvent was again evaporated to remove the boron as $B(OMe)_3$. MeOH was added and removed in this way twice more. To a dry residue chloroform was added and product was left to precipitate. A desired product was filtered off and dried to give compound **7a** (1.6 g, 65%) as a colorless solid.

^{1}H-NMR (DMSO-d_6): δ 10.37 (bs, 1H), 9.54 (bs, 2H), 8.35 (s, 1H), 7.49 (d, *J*=6.6, 1H), 7.23 (t, *J*=7.3, 1H), 6.99 (d, *J*=8.0, 1H), 6.93 (s, 2H), 6.84 (t, *J*=7.4, 1H), 4.20 (d, *J*=13.1, 1H), 4.12 (d, *J*=13.1, 1H), 3.79 (bs, 1H), 3.58 (bm, 1H), 3.33 (bs, 1H), 2.40 (s, 6H), 2.21 (s, 3H), 1.55 (d, *J*=6.45, 3H).

^{13}C-NMR (DMSO-d_6): δ 156.0 (C_{Ar}OH), 131.7, 131.5, 130.4, 130.1 (2x*C*), 119.0, 118.0, 115.4, 79.2, 51.5, 51.1, 42.6, 20.3, 18.0 (2x*C*), 14.3.

IR (KBr): 3154.0, 2957.3, 2725.9, 2406.7, 1598.7, 1575.1, 1459.4, 1393.8, 1270.4, 1245.3, 1185.0, 1131.5, 1105.9, 854.8, 757.4, 579.0, 497.5, 474.4.

MS(ESI): m/z calculated for $C_{19}H_{26}N_2O$ $[M+H]^+$ 299.2045, observed 299.2003.



(*S*)-1-(2-hydroxybenzyl)-3-mesityl-5-methyl-4,5-dihydro-1*H*-imidazol-3-ium chloride, 8a

A compound **7a** (1.0 g, 2.7 mmol) was suspended in dry toluene (30 mL), followed by addition of $(EtO)_3CH$ (5.5 mL). The reaction mixture was stirred at reflux temperature for 24 h. Afterwards the mixture was cooled down and solvent was removed by vacuum. To a dry residue chloroform (10 mL) was added and a white precipitate was filtered off and dried in vacuum to give compound **8a** (0.82g, 88%) as a colorless solid. M. p.: 268-269 ºC.

^{1}H-NMR (DMSO-d_6,): δ 10.25 (s, 1H), 8.90 (s, 1H), 7.36 (d, *J*=7.5, 1H), 7.23 (t, *J*=7.5, 1H), 7.04 (s, 2H), 6.99 (d, *J*=8.0, 1H), 6.85 (t, *J*=7.4, 1H), 4.85 (d, *J*=14.6, 1H), 4.58 (d, *J*=14.6, 1H), 4.27-4.21 (m, 2H), 3.79-3.74 (m, 1H), 2.27 (s, 3H), 2.24 (bs, 6H), 1.44 (d, *J*=6.0, 3H).

^{13}C-NMR (DMSO-d_6,): δ 159.0 (C_{Ar}OH), 156,4, 139.3, 135.5 (2x*C*), 131.0, 130.8, 129.3 (2x*C*), 119.2, 119.1, 115.6, 56.9, 55.7, 45.2, 20.5, 17.9, 17.1 (2x*C*).

^{1}H-NMR ($CDCl_3$): δ 8.98 (s, 1H), 7.41 (d, *J*=8.0, 1H), 7.15 (t, *J*=8.0, 1H), 7.05 (d, *J*=7.5, 1H), 8.86-6.76 (bs, 2H), 6.74 (t, *J*=7.5, 1H), 5.31 (d, *J*=14.0, 1H), 4.41 (d, *J*=14,0 1H), 4.32-4.23 (m, 1H), 4.14 (t, *J*=10.0, 1H), 3.60-3.53 (m, 1H), 2.27 (s, 6H), 2.23 (s, 1H), 1.48 (d, *J*=7.0, 3H).

IR (KBr): 3022.9, 2999.7, 2948.1, 2875.8, 2723.9, 2613.6, 1644.0, 1597.3, 1512.9, 1481.1, 1457.4, 1376.4, 1335.9, 1269.4, 1215.9, 1173.9, 1141.2, 1110.8, 1043.3, 994.1, 853.8, 756.4, 659.1, 577.6, 527.9.

MS (ESI): m/z calculated for $C_{20}H_{24}N_2O$ $[M-Cl]^+$ 309.1967, found 309.1977;

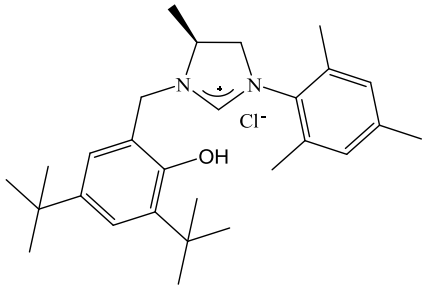
Anal. calcd: C 69.65, H 7.31, N 8.12, found: C 69.50, H 8.49, N 8.12.

The compound **7b** (*S*)-2,4-di-tert-butyl-6-{[1-(mesitylamino)propan-2-ylamino]methyl}-phenol dihydrochloride was obtained by the same procedure as **7a**. and used further (see synthesis of **8b**). The compounds **7c** and **7d** were obtained by the same procedure as **7a**, and their analytical data confirmed the identity and purity.

7c: MS(ESI): m/z calculated for $C_{19}H_{26}N_2O$ $[M+H]^+$ 299.2045, observed 299.2010.

7d: MS(ESI): m/z calculated for $C_{27}H_{42}N_2O$ $[M+H]^+$ 411.3297, observed 411.3307.

IR (KBr): 3184.8, 2960.7, 2741.2, 2391.7, 1701.7, 1584.1, 1554.6, 1518.8, 1482.1, 1440.1, 1393.9, 1362.2, 1282.1, 1224.2, 1202.7, 1169.9, 1125.9, 879.4, 853.4, 758.2.



(*S*)-1-(3,5-di-*tert*-butyl-2-hydroxybenzyl)-3-mesityl-5-methyl-4,5-dihydro-1*H*-imidazol-3-ium chloride, 8b

The mixture of a compound **3b** (1.5 g, 3.5 mmol) and a solution of BH_3·THF complex (1M, 20 mL) was stirred at reflux temperature for 24 h. Then the mixture was cooled down to room temperature and MeOH was added drop-wise till all bubbling ceased. Conc. HCl*aq* (12M, 1ml) was added and the solvent was removed by evaporation. The resulting solid was redissolved in MeOH and the solvent was again evaporated to remove the boron as $B(OMe)_3$. MeOH was added and removed and repeated twice. Dry residue was suspended in toluene (15 mL) and $(EtO)_3CH$ (6,5 mL) was added. The reaction mixture was stirred at reflux temperature for 14 hours. Afterwards the mixture was cooled down. A white precipitate was filtered off and washed with pentane to give compound **8b** (0.68 g, 42%) as a colorless solid. M. p.: 270-271 ºC. $[\alpha]_D^{20}$= -1.1 (2, MeOH).

^{1}H-NMR (DMSO-d_6): δ 8.95 (s, 1H, NC*H*N), 8.85 (s, 1H, O*H*), 7.25 (s, 1H, Ar*H*), 7.21 (s, 1H, Ar*H*), 7.04 (s, 2H, Ar*H*), 5.20 (d, *J*=15.0, 2H), 4.87 (d, *J*=15.0, 2H), 4.28-4.17 (m, 2H), 3,80-3.74 (m, 1H), 2.26 (bs, 9H), 1.41 (d, *J*=5.8, 3H), 1.38 (s, 9H), 1.27 (s, 9H).

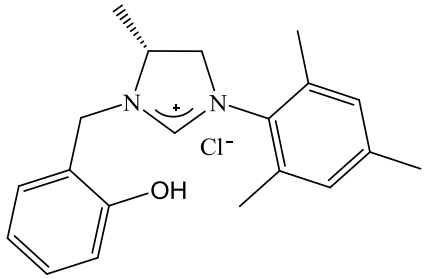
^{13}C-NMR (DMSO-d_6): δ 158.2, 151.7 (C_{Ar}OH), 142.1, 139.2, 138.5, 135.5, 131.0, 129.3, 124.9, 123.4, 122.2, 56.8, 56.1, 45.9, 34.7, 33.9, 31.3, 29.7, 20.5, 17.9, 17.0.

IR (KBr): 3004.6, 2949.6, 1636.3, 1481.1, 1444.9, 1361.0, 1291.6, 1251.6, 1223.1, 1133.9, 991.7, 850.5, 693.3, 573.2.

MS(ESI): m/z calculated for $C_{28}H_{41}N_2O$ $[M]^+$ 421.3219, observed 421.3258.

Anal. calcd: C 73.57, H 9.04, N 6.13, found: C 73.81, H 9.13, N 6.06.

Compounds **8c** and **8d**, which are the enantiomers of **8a** and **8b**, respectively, were obtained from Boc-D-alanine by the same procedures as their *S* analogues. The small chemical shift differences in the ^{1}H NMR spectra within pairs of enantiomers were observed and discussed in results and discussion section.

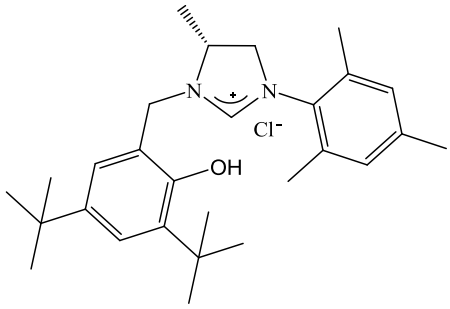


(*R*)-1-(2-hydroxybenzyl)-3-mesityl-5-methyl-4,5-dihydro-1*H*-imidazol-3-ium chloride, 8c

^{1}H-NMR (DMSO-d_6,): δ 10.40 (s, 1H), 8.99 (s, 1H), 7.36 (d, *J*=6.1, 1H), 7.22 (t, *J*=8.0, 1H), 7.06 (d, *J*=8.0, 1H), 7.03 (s, 2H), 6.84 (t, *J*=6.6, 1H), 4.89 (d, *J*=14.6, 1H), 4.58 (d, *J*=14.6, 1H), 4.30-4.17 (m, 2H), 3.79-3.74 (m, 1H), 2.27, 2.24 (s, 9H), 1.44 (d, *J*=6.1, 3H).

^{13}C-NMR (DMSO-d_6,): δ 159.0 (C_{Ar}OH), 156.5, 139.2, 135.5 (2x*C*), 131.0, 130.71, 130.1, 129.3 (2x*C*), 119.1, 115.7, 56.9, 55.7, 45.1, 20.5, 17.9, 17.1 (2x*C*).

Anal. calcd: C 69.65, H 7.31, N 8.12, found: C 68.94, H 7.11, N 8.11.

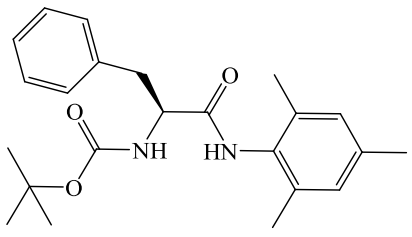


(*R*)-1-(3,5-di-*tert*-butyl-2-hydroxybenzyl)-3-mesityl-5-methyl-4,5-dihydro-1*H*-imidazol-3-ium chloride, 8d

^{1}H-NMR (DMSO-d_6): δ 9.00 (s, 1H), 8.93 (s, 1H), 7.23 (d, *J*=2.4, 1H), 7.21 (d, *J*=2.5, 1H), 7.03 (s, 2H), 5.23 (d, *J*=14.9, 1H), 4.82 (d, *J*=14.9, 1H), 4.26-4.17 (m, 2H), 3.78-3.74 (m, 1H), 2.26 (s, 9H), 1.41 (d, *J*=6.0, 3H), 1.37 (s, 9H), 1.27 (s, 9H).

^{13}C-NMR (DMSO-d_6,): δ 158.1 (C_{Ar}OH), 151.8, 141.9, 139.2, 138.5, 135.5 (2x*C*), 130.9, 129.3 (2x*C*), 124.9, 123.4, 122.2, 56.7, 55.9, 45.9, 34.7, 33.9, 31.3, 29.7, 20.4, 17.9, 17.1 (2x*C*).

MS(ESI): m/z calculated for $C_{28}H_{41}N_2O[M]^+$ 421.3219, observed 421.3074.



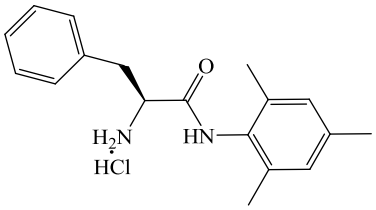
(*S*)-*N*-(1-(mesitylamino)-1-oxo-3-phenylpropan-2-yl)-3,3-dimethylbutanamide, 9

2,4,6-Trimethylaniline (2.7 mL, 20 mmol) was added to a solution of Boc-L-alanine (5.3 g, 20 mmol) in dry THF (100 mL), followed by addition of DCC (4.1 g, 20 mmol) solution in dry THF (20 mL). The mixture was stirred at room temperature for 18 h.

Subsequently white precipitate was filtered off and filtrate was concentrated by using a rotary evaporator. The oily filtrate residue was purified by crystallization in ethyl acetate to give compound **9** (5.6 g, 74%, 2 steps) as a colorless solid.

^{1}H-NMR ($CDCl_3$): δ 7.45 (s, 1H, N*H*), 7.31-7.21 (m, 5H), 6.79 (s, 2H), 5.25 (d, *J*=7.6, 1H), 4.57 (q, *J*=7.40 1H), 3.22-3.08 (m, 2H), 2.22 (s, 3H), 1.96 (s, 6H), 1.42 (s, 9H).

^{13}C-NMR ($CDCl_3$): δ 170 (*C*O), 136.9, 136.8, 135.1 (2x*C*), 130.7, 129.5 (2x*C*) 128.8, 128.7, 126.9, 80.4, 56.1, 37.8, 28.3 (3x*C*), 20.9, 18.1 (2x*C*).

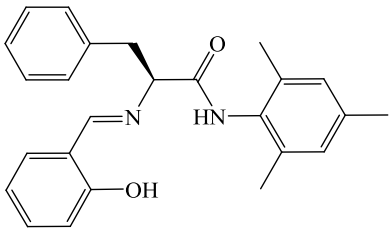


(*S*)-2-amino-*N*-mesityl-3-phenylpropanamide hydrochloride, 10

A solution of a compound **9** (4.0 g, 10.0 mmol) and a solution of HCl in diethyl ether (1M, 65 mL) was stirred for 15 h. Afterwards a white precipitate was filtered off and washed with diethyl ether to give compound **10** (2.8 g, 84%) as a colorless solid.

^{1}H-NMR (DMSO-d_6): δ 10.19 (s, 1H), 8.56 (bs, 3H), 7.41 (d, *J*=7.2, 2H), 7.34 (t, *J*=7.2, 2H), 7.29-7.26 (m, 1H), 6.82 (s, 2H), 4.42 (t, *J*=7.4, 1H), 3.27-3.23 (m, 1H), 3.18-3.14 (m, 1H), 2.20 (s, 3H), 2.00 (bs, 6H).

^{13}C-NMR (DMSO-d_6): δ 166.5, 135.7, 135.2 (2x*C*), 134.7, 131.3, 129.6 (3x*C*), 128.5 (2x*C*), 128.3 (2x*C*), 127.1, 53.5, 37.2, 20.4, 18.0 (2x*C*).



(*S*)-2-(2-hydroxybenzylideneamino)-*N*-mesityl-3-phenylpropanamide, 11

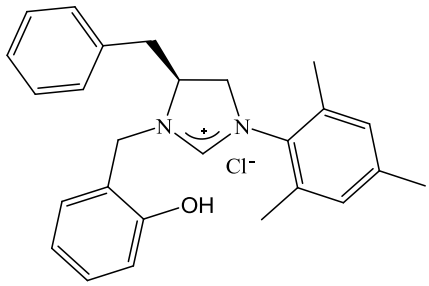
MeONa was added to a solution of compound **10** (2.8 g, 8.8 mmol) in MeOH (35 mL) until reaction mixture gained neutral pH. Afterwards salicylaldehyde (0.95 mL, 8.8 mmol) was added and the resulting mixture was stirred at room temperature for 20 h. A yellow precipitate was filtered off and washed with water (100 mL) and hexane (40 ml), followed by crystallization in ethyl acetate to give compound **11** (2.4 g, 70%) as a yellow solid.

^{1}H-NMR ($CDCl_3$): δ 12.42 (s, 1H, O*H*), 7.99 (s, 1H, C*H*=N), 7.40 (bs, 1H, N*H*), 7.36-7.31 (m, 1H), 7.26-7.20 (m. 2H), 7.18 (m, 3H), 7.12 (dd, *J*=7.5, 1.6, 1H), 6.97 (d, *J*=8.2, 1H), 6.87 (td, *J*=8.3, 7.6, 1H), 6.85 (s, 2H, ArH_{Mes}), 4.24-4.20 (m, 1H), 3.52-3.48 (m, 1H), 3.25-3.20 (m, 1H), 2.24 (s, 3H), 2.07 (s, 6H).

^{13}C-NMR ($CDCl_3$): δ 169.1 (*C*O), 167.8 (*C*H=N), 160.5, 137.0, 136.8, 134.8 (2x*C*), 133.3, 132.2, 130.5 (3x*C*), 129.9 (2x*C*), 128.9 (2x*C*), 128.5, 126.9, 119.3, 118.3, 117.0, 75.6, 41.0, 20.9, 18.2 (2x*C*).

IR (KBr): 2921.3, 2858.2, 1671.7, 1632.9, 1524.4, 1482.8, 1360.2, 1280.4, 1247.5, 1194.8, 1151.5, 1032.0, 922.5, 857.0, 762.3, 737.4, 697.1, 437.5.

Anal. calcd: C 77.69, H 6.78, N 7.25, found: C 77.71, H 6.98, N 7.25.



(*S*)-4-benzyl-3-(2-hydroxybenzyl)-1-mesityl-4,5-dihydro-1*H*-imidazol-3-ium chloride, 13

The mixture of a compound **11** (2.3 g, 6.0 mmol) and a solution of BH_3·THF complex (1M, 35 mL) was stirred at reflux temperature for 14 h. Then the mixture was cooled down to room temperature and MeOH was added drop-wise till all bubbling ceased. Conc. HCl*aq* (12M, 1mL) was added and the solvent was removed by evaporation. The resulting solid was redissolved in MeOH and the solvent was again evaporated to remove the boron side product $B(OMe)_3$. MeOH was added and removed in this way twice more. A dry residue (containing not isolated compound **12**) was suspended in toluene (40 mL) and then $(EtO)_3CH$ (6.5 mL) was added. The reaction mixture was stirred at reflux temperature for 14 h. Afterwards the mixture was cooled down. A white precipitate was filtered off, washed with diethyl ether and dried in vacuum. Then a white solid was crystallized from DCM/pentane to give compound **13** (0.90 g, 38%) as a colorless solid.

$[\alpha]_D^{20}$ = + 44.7. (1, MeOH).

^{1}H-NMR (DMSO-d_6): δ 10.44 (s, 1H, O*H*), 8.97 (s, 1H, NC*H*N), 7.38-7.34 (m, 3H), 7.33-7.28 (m, 3H), 7.26 (td, *J*=7.8, 1.6, 1H), 7.05 (d, *J*=7.7, 1H), 6.97 (bs, 2H, ArH_{Mes}), 6.86 (t, *J*=7.4, 1H), 5.00 (d, *J*=14.5, 1H), 4.72 (d, *J*=14.5, 1H), 4.46-4.38 (m, 1H), 4.19 (t, *J*=11.8, 1H), 3.78 (dd, J=8.10, 11.80, 1H), 3.27-3.16 (m, 2H), 2.23 (s, 3H), 2.16 (bs, 3H), 1.82 (bs, 3H).

^{13}C-NMR (DMSO-d_6): δ 159.6 (NCHN), 156.6 (*C*OH), 139.3, 135.4, 135.0 (2x*C*), 131.1, 130.8, 130.3, 129.9(2x*C*), 129.2 (2x*C*), 128.8 (2x*C*), 127.2, 119.1, 118.9, 115.7, 59.7, 54.1, 45.7, 35.7, 20.5, 17.2, 16.5.

IR (KBr): 2952.2, 1644.2, 1600.8, 1497.1, 1478.9, 1458.2, 1378.1, 1285.2, 1228.2, 1213.9, 1134.4, 760.1, 739.4, 704.5, 535.5.

MS (ESI): m/z calculated for $C_{26}H_{29}N_2O$ [M-Cl]+ 385.2280, observed 385.2287.

Anal. calcd: C 74.18, H 6.94, N 6.66, found: C 73.49, H 6.78, N 6.52.

Further purification of the filtrate using silica gel chromatography (DCM/MeOH) afforded the by-product **14**. The attempts to identify it by NMR and MS did not provide conclusion on its structure.

^{1}H-NMR ($CDCl_3$): δ 8.48 (bs, 1H), 7.46 (s, 1H), 7.24-7.13 (m, 7H), 6.95 (d, *J*=8.0, 1H), 6.83 (t, *J*=7.4, 1H), 6.76 (s, 1H), 6.71 (s, 1H), 3.38 (d, J=14.0, 1H), 3.21 (dd, *J*=18.2; 13.5, 2H), 3.15 (d, *J*=14.0, 1H), 2.19 (s, 3H), 1.61 (s, 1H), 1.49 (s, 3H), 1.09 (s, 3H).
^{13}C-NMR ($CDCl_3$): δ 180.9, 155.9, 155.7, 139.2, 135.7, 135.6 (2x*C*), 134.6, 132.6, 130.7, 129.3, 129.2, 129.1, 128.3, 127.8, 127.3, 122.3, 120.8, 118.5, 77.2, 42.4, 40.8, 20.5, 17.3, 16.7.

^{1}H-NMR (DMSO-d_6): δ 9.19 (s, 1H), 7.86 (s, 1H), 7.27-7.15 (m, 4H), 7.14-7.10 (m, 2H), 7.05 (t, *J*=7.5, 1H), 6.81-6.77 (m, 2H), 6.75 (bs, 1H), 6.72 (t, *J*=7.5, 1H), 3.20 (d, J=14.0, 1H), 3.17-3.08 (m, 3H), 2.16 (s, 3H), 1.52 (s, 3H), 1.03 (s, 3H).
^{13}C-NMR (DMSO-d_6):δ 180.9 (*C*ON), 155.9, 153.9, 137.9, 135.4 (2x*C*), 135.2, 132.4, 130.5, 128.7, 128.6 (2x*C*), 128.0, 127.9, 126.7, 121.7, 118.7, 115.6, 75.7, 41.5, 36.8, 20.4, 16.9, 16.4.
MS(ESI): m/z observed; 439.1944.
Anal.; found: C 67.30, H 7.02, N 5.86.

^{1}H and ^{13}C assignments of the compounds 8a and 8b and 13

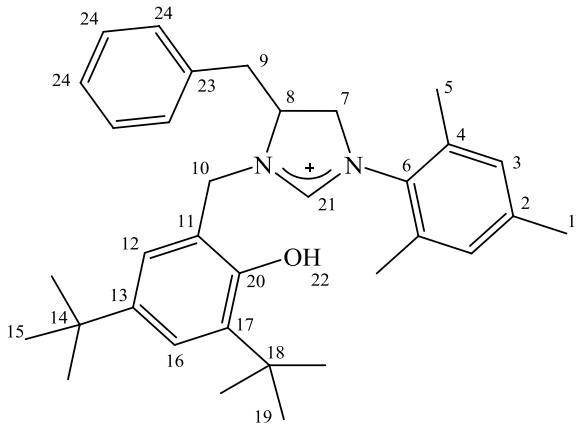


Table 3.1 ^{1}H and ^{13}C assignments of the compounds **8a** and **8b** and **13** at 295K in DMSO-d_6

	8a		**8b**		**13**	
Atom label	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
1	2.27	20.5	2.26	17.1 or 20.5	2.23	20.5
2	-	139.3	-	139.2	-	139.3
3	7.04	129.3	7.04	129.4	6.97	129.2
4	-	135.5	-	135.5	-	135.0
5	2.24	17.1	2.26	17.1 or 20.5	1.82, 2.16	17.1, 16.5
6	-	131.0	-	131.1	-	131.1
7	3.79-3.74, 4.27-4.21	56.9	3.80-3.74, 4.28-4.17	56.8	3.80-3.75, 4.18	54.1
8	4.27-4.21	55.7	4.28-4.17	56.1	4.45-4.43	59.7
9	1.44	17.9	1.40	17.9	3.26-3.16	35.7
10	4.85, 4.58	45.2	5.20, 4.87	45.8	4.73, 5.00	45.7
11	-	119.1	-	122.2	-	119.1
12	7.36	130.8	7.21	124.9	7.40-7.34	130.8
13	6.85	119.2	-	142.1	6.85	118.9
14	-	-	-	33.9	-	-
15	-	-	1.27	31.35	-	-
16	7.23	130.2	7.25	123.5	7.25	130.3
17	6.99	115.6	-	138.6	7.05	115.7
18	-	-	-	34.8	-	-
19	-	-	1.38	29.7	-	-
20	-	156.4	-	151.7	-	156.6
21	8.90	159.0	8.95	158.2	8.97	159.6
22	10.25	-	8.85	-	10.44	-
23	-	-	-	-	-	135.4
24	-	-	-	-	7.40-7.34, 7.32-7.28	129.9, 128.8, 130.8

3.3.2 Coordination of ligand 8a to metal complexes

3.3.2.1 Coordination of ligand 8a to Ru(II) complex 15

NMR scale experiment: A 10 mL vial was charged with ligand **8a** (10 mg, 0.029 mmol) and compound **15** (16 mg, 0.019 mmol). Afterwards dry toluene (0.8 mL) was added, followed by addition of a solution of KHMDS in toluene (1M, 0.12 mL, 0.060 mmol). The mixture was stirred for 5 minutes, thereafter 0.7 mL of this solution was transferred in a NMR tube. Additionally, a probe with $CDCl_3$ was placed into the NMR tube as calibration lock. ^{31}P NMR measurements were recorded after 0.5h, 1h, 2h, 4h, 6h, 21h.

General procedure: A 15 mL vial was charged with ligand **8a** (50 mg, 0.145 mmol) and compound **15** (79 mg, 0.096 mmol). Afterwards dry toluene (2.5 mL) was added followed by addition of KHMDS solution in toluene (1M, 0.58 mL, 0.290 mmol). The mixture was stirred under argon and after 0.5h, 1h, 2h, 4h, 6h, 21h. 0.5 mL samples were taken and dried. Afterwards dry samples were dissolved in $CDCl_3$ and ^{1}H and ^{31}P NMR spectra were recorded.

3.3.2.2 Coordination of ligand 8b to Ru(II) complex 15

NMR scale experiment: A 10 mL vial was charged with ligand **8b** (10 mg, 0.021 mmol) and compound **15** (13 mg, 0.014 mmol). Dry toluene (0.8 mL) was added, followed by addition of a solution of KHMDS in toluene (1M, 0.12 mL, 0.060 mmol). The mixture was stirred for 5 min and afterwards 0.7 mL of this solution was transferred in a NMR tube. Additionally a probe with $CDCl_3$ was placed into the NMR tube as calibration lock. ^{31}P NMR measurements were recorded after 0.5h, 1h, 2h, 4h, 6h, 21h.

3.3.2.3 Coordination of ligand 8a to Ru(II) complex 19

Variant I: A 15 mL vial was charged with ligand **8a** (30 mg, 0.087 mmol), compound **19** (83 mg, 0.087mmol) and NaH (4 mg, 0.174 mmol), followed by addition of dry THF (2 mL).

Variant II: A 15 mL vial was charged with ligand **8a** (0.10 g, 0.29 mmol), compound **19** (0.28 g, 0.29 mmol), followed by addition of dry toluene (3 mL) and a solution of KHMDS in toluene (1M, 2.5 mL).

Variant III: A 15 mL vial was charged with ligand **8a** (30 mg, 0.087 mmol), compound **19** (63 mg, 0.066 mmol) and *t*BuOK (15 mg, 0.132 mmol), followed by addition of dry THF (2 mL).

The reaction mixtures were stirred under argon at room temperature for 24 h. Afterwards the mixtures were dried and flash silica gel chromatography was performed (DCM/*i*PrOH).

3.3.2.4 Coordination of ligand 8a to Ru(II) complex 16

Variant I: A 50 mL flask was charged with ligand **8a** (0.10 g, 0.29 mmol) and compound **16** (0.25 g, 0.27 mmol). Afterwards, dry toluene (15 mL) and a solution of KHMDS in toluene (1M, 2.5 mL) were added. The reaction mixture was stirred at room temperature for 12 hours, heated to 80 ºC and maintained at this temperature for 3 hours. All manipulations were carried out under argon. The mixture was then cooled to room temperature and filtered off through a Celite 512 layer. The filtrate was concentrated and dried. Flash silica gel chromatography (DCM/*i*PrOH) enabled separation of product **20**.

Variant II: A 50 mL flask was charged with ligand **8a (**0.10 g, 0.29 mmol) and compound **16** (0.25 g, 0.27 mmol). Afterwards, dry toluene (15 mL) and a solution of KHMDS in toluene (1M, 2.5 mL) were added. The reaction mixture was stirred at room temperature for 36 hours. All manipulations were carried out under argon. Thereafter, the mixture was filtered off through a Celite 512 layer and then the filtrate was concentrated and dried. Flash silica gel chromatography (DCM/*i*PrOH) enabled the separation of the red product. The product was purified by several precipitations from toluene-pentane and finally its ^{1}H NMR spectrum (Fig.2.14 c) and mass spectrum were recorded. According to mass spectrum the isolated red product **21** is the mixture of mononuclear complex and dinuclear diruthenium complexes.
Two peaks observed in mass spectrum correspond to {[(**8a**-H)$^-$]$_2$Ru(Ind) + H$^+$} (calculated for $C_{55}H_{56}N_4O_2Ru+H^+$ 907.3252, observed 907.3498) and to {[(**8a**-H)$^-$]$_2$Ru(Ind)}$_2$ + H$^+$ (calculated for for $C_{110}H_{112}N_8O_4Ru_2+H^+$ 1813.697, observed 1813.6917).

3.3.2.5 Coordination of ligand 8a to Rh(I) complex 22

Variant I: A 25 mL flask was charged with ligand **8a** (100 mg, 0.29 mmol) and *t*BuOK (70 mg, 6 mmol) and toluene (9 mL). Afterwards complex **22** (72 mg, 0.15 mmol) was added. The resulting reaction mixture was stirred at room temperature for 24 hours. Then mixture was filtered off through a Celite 512 layer and washed with DCM (5 mL). The filtrate was concentrated and purified *via* flash silica gel chromatography (DCM/MeOH). The mixture of extended *cis* and extended *trans* isomers was isolated as a yellow powder (86 mg, molar ratio 4:1).

Variant II: A 25 mL flask was charged with ligand **8a** (0.20 g, 0.58 mmol) and *t*BuOK (0.24 g, 1.6 mmol) and chloroform (10 mL), washed through basic Al_2O_3 (grade I) before use. After ca 10 min complex **22** (0.14 g, 0.29 mmol) was added. The resulting yellow reaction mixture was stirred at 45 ºC for 5 h and afterwards at room temperature for 24 h. Then mixture was filtered off through a Celite 512 layer and washed with DCM (10 mL). The filtrate was concentrated and purified *via* flash silica gel chromatography (DCM/*i*PrOH). The mixture of extended *cis* and extended *trans* isomers was isolated as a yellow powder (0.16 g, molar ratio 5:1).
Major isomer: ^{1}H-NMR ($CDCl_3$): δ 8.05 (s, 1H), 7.13 (t, *J*=8.0, 1H), 6.97-6.90 (m, 3H), 6.82 (d, *J*=8.0, 1H), 6.73 (t, *J*=8.0, 1H), 3.97 (d, *J*=13.5, 1H), 3.90 (d, *J*=13.5, 1H), 3.88-3.81

(m, 1H), 3.34-3.30 (m, 1H), 2.97-2.89 (m, 1H), 2.29 (s, 3H), 2.22 (s, 3H), 2.18 (s, 3H), 1.17 (d, *J*=6.5, 3H).

3.3.2.6 Coordination of ligand 8a to Pd(II) complex

Variant I: $PdCl_2$ (10 mg, 0.06 mmol) was suspended in pyridine-d_5 (1 mL) and stirred at 60 ºC for 6 h. After cooling the resulting yellow mixture to room temperature ligand **8a** (20 mg, 0.06 mmol) was added, followed by addition of K_2CO_3 (50 mg, 0.36 mmol). After one hour the yellow mixture turned orange. The reaction mixture was stirred at room temperature for 16 h. Afterwards, the mixture was filtered off through a Celite 512 layer and a ^{1}H NMR spectrum was recorded.

Variant II: $PdCl_2$ (50 mg, 0.29 mmol) was suspended in pyridine (3 mL) and stirred at 60 ºC for 6 h. After cooling the resulting yellow mixture to room temperature ligand **8a** (98 mg, 0.29 mmol) was added, followed by addition of K_2CO_3 (155 mg, 1.12 mmol). After one hour yellow mixture turned orange. The reaction mixture was stirred at room temperature for 16 h. Afterwards, the mixture was filtered off through a Celite 512 layer and the filtrate was concentrated using vacuum. Separation *via* flash silica gel chromatography (DCM/*i*PrOH) afforded a mixture of unidentified compounds.

3.3.3 Synthesis of modified PAMAM dendrimers

Synthesis of 3rd generation PAMAM dendrimer G3-PAMAM(-NH_2)$_{32}$

The 3rd Generation PAMAM dendrimer **G3-PAMAM(-NH_2)$_{32}$** was prepared according to Tomalia`s procedure[173] using ethylenediamine as a core and a building block. M = 6907.9 Da. ^{1}H-NMR (CD_3OD): δ 4.82 (s), 3.28-3.22 (m, 120H), 2.84-2.75 (m, 120H), 2.75-2.49 (m, 64H), 2.61-2.54 (m, 60H), 2.40-2.32 (m, 120H).

Synthesis of dendrimer G3-PAMAM(-NH_2)$_{32}$ with salicylaldehyde:

Variant I using 16 equivalent of salicylaldehyde:
Dendrimer **G3-PAMAM(-NH_2)$_{32}$** (300 mg, 43 μmol) was dissolved in methanol (0.8 mL). Afterwards salicylaldehyde (73 μL, 690 μmol) was added. The reaction mixture was stirred

at room temperature for 3 h and the solvent was removed using vacuum to give **G3-PAMAM(-NH_2)$_{32}^{50Sal}$**.

^{1}H-NMR (DMSO-d_6): δ 8.45 (bs, 15H), 8.11-7.92 (m, 26H), 7.91-7.68 (m, 38H), 7.37 (bs, 15H), 7.26 (bs, 15H), 6.82 (bs, 31H), 3.58 (bs, 34H), 3.34 (bs, 36H), 3.13-3.02 (m, 92H), 2.73-2.52 (m, 138H), 2.41 (bs, 58H), 2.15 (bs, 120H).

Variant II using 32 equivalent of salicylaldehyde:

Dendrimer **G_3-PAMAM(-NH_2)$_{32}$** (1.00 g, 0.14 mmol) was dissolved in methanol (2 mL). Afterwards salicylaldehyde (0.49 mL, 4.6 mmol) was added. The reaction mixture was stirred at room temperature for 3 h and the solvent was removed using vacuum to give **G3-PAMAM(-NH_2)$_{32}^{100Sal}$**.

^{1}H-NMR (DMSO-d_6): δ 8.38 (bs, 25H), 7.32 (bs, 25H), 7.23 (bs, 25H), 6.79 (bs, 50H), 3.53 (bs, xH), 3.31 (bs, 60H), 3.14-2.97 (m, 69H), 2.73-2.54 (m, 118H), 2.46-2.29 (m, 64H), 2.15 (bs, 120H).

Immobilization of Ru(II) complex 15 on a G3-PAMAM(-NH_2)$_{32}^{50Sal}$

G3-PAMAM(-NH_2)$_{32}^{50Sal}$ (50 mg) was dissolved in MeOH (2 mL). Afterwards ruthenium complex **15** (82 mg, 0.97 mmol) dissolved in dry THF (2 mL) was added. Reaction mixture was stirred under argon for 24 h. Afterwards the dark purple mixture was concentrated to ca 1/3 volume and filtered off. The resulting purple solid was washed with THF and pentane and then dried in vacuum.

Immobilization of Ru(II) complex 15 on a G3-PAMAM(-NH_2)$_{32}^{100Sal}$

Dendrimer **G3-PAMAM(-NH_2)$_{32}^{100Sal}$** (45 mg) was dissolved in $CHCl_3$ (30 mL). Afterwards complex **15** (55 mg, 0.065 mmol) dissolved in dry THF (2 mL). The reaction mixture was stirred under argon for 24 h. Afterwards the dark purple mixture was concentrated to ca 1/8 volume and filtered off. The resulting purple solid was washed with THF and pentane and then dried in vacuum. After washing the color of the solid turned to green.

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Abstract

The research presented in this thesis concerns mainly synthesis and development of chiral, bidenatate *N*-heterocyclic carbene precursors and their potential utilization as ancillary ligands for Ru(II), Rh(I), Pd(II) complexes. Since chiral imidazolinium salts are having remarkable applications in the area of asymmetric synthesis the usage of chiral Boc-protected amino acids: L-alanine and L-phenylalanine as starting materials and stereogenic center providers were introduced. The experimental work done in this thesis was divided into three parts.

In a first part two synthetic routes leading to imidazolinium salts: (*S*)-3-(2-hydroxybenzyl)-1-mesityl-4-methyl-5-oxo-4,5-dihydro-1*H*-imidazol-3-ium chloride **5a** and (*S*)-3-(3,5-di-*tert*-butyl-2-hydroxybenzyl)-1-mesityl-4-methyl-5-oxo-4,5-dihydro-1*H*-imidazol-3-ium chloride **5b**, (*S*)- and (*R*)-1-(2-hydroxybenzyl)-3-mesityl-5-methyl-4,5-dihydro-1*H*-imidazol-3-ium chlorides **8a** and **8c**, (*S*)- and (*R*)-1-(3,5-di-*ter*t-butyl-2-hydroxybenzyl)-3-mesityl-5-methyl-4,5-dihydro-1*H*-imidazol-3-ium chlorides **8b** and **8d**, and (*S*)-4-benzyl-3-(2-hydroxybenzyl)-1-mesityl-4,5-dihydro-1*H*-imidazol-3-ium chloride **13** were proposed and their syntheses were described. Although the synthetic route to salt **5** occurred to be troublesome and gave mixture of isomers and by-products the route to salts **8a-d** and **13** with L-alanine and L-phenylalanine in the heterocycle backbone, respectively, gave desired imidazolinium salts and we were able to isolate them with good total yield. Obtained final compounds **8a-d** and **13** were fully characterized. This synthetic route could serve as useful method of obtaining such class of compounds.

Second part of this dissertation was focused on the coordination of the obtained saturated *N*-heterocyclic carbene ligand **8a** to selected Ru(II), Rh(I), and Pd(II) complexes. Coordination to the known metathesis reaction Ru-catalysts bis(tricyclohexylphosphine)-benzylidine ruthenium(II) dichloride **15** and bis(tricyclohexylphosphine)-3-phenyl-1*H*-inden-1-ylideneruthenium(II) dichloride **16** and to tris(triphenylphosphine) ruthenium(II) dichloride **19** by in situ deprotonation of the NHC salt in presence of strong bases should give easy access to novel bidentate NHC-Ru catalysts. Hovewer only promising results were obtained with complex **16** when KHMDS was used as a base. All other experiments led to undefined mixture of products.

In case of Rh-complexes, we used bis(1,5-cyclooctadiene)dirhodium (I) dichloride complex (**23**) as starting material and we were able to isolate mixture of two isomers, probably extended *cis* and extended *trans* dirhodium complexes in a molar ratio 5:1.
Coordination to palladium(II) lead to mixture of products as well.
Concluding, usage of obtained class of NHC precursors as ancillary ligands for Ru, Rh and Pd complexes leads to mixture of products, that are difficult for separation due to chemical resemblance (Rh, Pd) or quick decomposition (Ru).

In a third part attempts to obtain Ru-catalysts immobilized on a periphery modified 3rd generation PAMAM dendrimer were described. The synthesis of 3rd generation PAMAM dendrimers is a known divergent method. Condensation of outer -NH_2 groups with salicyl aldehyde easily provided PAMAM dendrimers with Schiff bases on their surface. The amount of consumed -NH_2 groups could be monitored by ^{1}H NMR experiments. Coordination of Ru complex **15** to modified dendrimer gave catalyst in a form of violet powder. This however showed poor catalytic activity towards standard RCM (Ring Closing Metathesis) reaction of diethyl diallyl malonate.

Keywords: chiral *N*-heterocyclic carbenes, Ru-complexes, modified PAMAM dendrimers

Streszczenie

W przedstawionej pracy opisano badania nad otrzymaniem chiralnych, bidentnych prekursorów *N*-heterocyklicznych karbenów w postaci soli imidazoliniowych oraz zbadanie możliwości ich zastosowania jako potencjalnych bidentnych ligandów kompleksów Ru(II), Rh(I) i Pd(II). Jako materiał wyjściowy do otrzymania soli imidazoliniowych posiadających centrum stereogeniczne zastosowano chiralne aminokwasy L-alaninę oraz L-fenyloalaninę w których grupa aminowa zablokowana jest grupą tert-butoksykarbonylową (Boc).
Część badawcza pracy została podzielona na trzy części.

W pierwszej części zaplanowano i opisano dwie ścieżki syntetyczne prowadzące do otrzymania następujących soli imidazoliniowych: chlorku (*S*)-3-(2-hydroksybenzylo)-1-mesitylo-4-methylo-5-oxo-4,5-dihydro-1*H*-imidazolu **5a** i chlorku (*S*)-3-(3,5-di-*tert*-butylo-2-hydroksybenzylo)-1-mesitylo-4-methylo-5-oxo-4,5-dihydro-1*H*-imidazolu **5b** oraz chlorki (*S*)- i (*R*)-1-(2-hydroksybenzylo)-3-mesitylo-5-methylo-4,5-dihydro-1*H*-imidazolu **8a** i **8c**, chlorki (*S*)- i (*R*)-1-(3,5-di-*tert*-butylo-2-hydroksybenzylo)-3-mesitylo-5-methylo-4,5-dihydro-1H-imidazolu **8b** i **8d** i chlorku (*S*)-4-benzylo-3-(2-hydroksybenzylo)-1-mesitylo-4,5-dihydro-1*H*-imidazolu **13**. W pięcioetapowej syntezie otrzymano z dobrą całkowitą wydajnością sole **8a-d** oraz **13** z odpowiednio Boc-L alaniny, Boc-D-alaniny oraz Boc-L-fenyloalaniny. Otrzymane produkty końcowe **8a-d** oraz **13** zostały scharakteryzowane za pomocą spektroskopii NMR, MS oraz IR. Opisana ścieżka syntetyczna może zostać wykorzystana do otrzymywania tej grupy związków. W reakcji pochodnych: chlorowodorku (*S*)-2-(2-hydroksybenzylamino)-*N*-mesitylopropanamidu **4a** oraz chlorowodorku (*S*)-2-(3,5-di-*tert*-butyl-2-hydroksybenzylamino)-*N*-mesitylopropanamidu **4b** z ortomrówczanem trietylu otrzymywano mieszaninę izomerów lub inne produkty uboczne.

W części drugiej opisano próby zastosowania otrzymanej soli **8a** jako bidentnego liganda wybranych kompleksów Ru(II), Rh(I) oraz Pd(II). Jako związki wyjściowe zastosowano znane rutenowe katalizatory reakcji metatezy olefin: dichlorek bis(tricykloheksylofosfino)benzylideno rutenu(II) **15** i dichlorek bis(tricykloheksylofosfino)-3-phenyl-1*H*-inden-1-ylideno rutenu(II) **16** oraz kompleks dichlorku tris(trifenylofosfiny) rutenu(II) **19**. Zastosowano metodę deprotonowania *in situ* otrzymanej soli **8a** w obecności silnej zasady. Planowano otrzymać nowe katalizatory rutenowe z bidentnym ligandem NHC koordynującym do atomu metalu za pomocą atomów C i O. Obiecujące wyniki otrzymano

w reakcji kompleksu **16** z ligandem **8a** w obecności KHMDS (heksametylenodisilazian potasu). We wszystkich innych eksperymentach uzyskiwano niezdefiniowaną mieszaninę produktów. Jako materiał wyjściowy do otrzymywania kompleksów rodu wykorzystano dichlorek bis(1,5-cyklooctadienu)dirodu(I) **23**. Wyizolowano mieszaninę izomerów, najprawdopodobniej kompleksów dirodu *cis* i *trans* w stosunku molowym 5:1.

Próby koordynacji liganda **8a** do kompleksów Pd(II) prowadziły do otrzymywania mieszaniny produktów, której nie udało się rozdzielić.

Podsumowując, zastosowanie otrzymanych prekursorów *N*-heterocyklicznych karbenów jako ligandów Ru, Rh i Pd prowadzi do otrzymania mieszaniny produktów, które są trudne do wyizolowania ze względu na chemiczne podobieństwo (Rh, Pd) lub ze względu na szybki rozkład otrzymanych związków (Ru).

W części trzeciej opisano próby immobilizacji katalizatora rutenowego na peryferycznie zmodyfikowanym dendrymerze typu PAMAM 3-ciej generacji. Dendrymer typu PAMAM 3-ej generacji otrzymano stosując znaną metodę rozbieżną. W wyniku kondensacji peryferyjnych grup NH_2 dendrymeru z aldehydem salicylowym otrzymano dendrymery z zasadami Schiffa na zewnętrznej powierzchni dendrymeru. Ilość utworzonych zasad w stosunku do nieprzereagowanych grup NH_2 oznaczano za pomocą spektroskopii ^{1}H NMR. W reakcji zmodyfikowanego dendrymeru i kompleksu rutenu **15** otrzymywano katalizator w postaci fioletowego proszku. Otrzymany katalizator wykazywał słabą aktywność katalityczną w reakcji metatycznego zamykania pierścienia, RCM (Ring Closing Metathesis) diallilomalonianu dietylu.

Słowa kluczowe: chiralne karbeny *N*-heterocykliczne, kompleksy rutenu, modyfikowane dendrymery PAMAM

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